Contents

Clostridium Difficile Infection

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Many infections have emerged with increased virulence in the recent years. Clostridium difficile infection causes disease in presence of exposure to antibiotics either during or after treatment. It has become an increasingly important nosocomial infection throughout the western world over recent years. It results in antibiotic-associated diarrhoea, antibiotic-associated colitis and pseudo-membranous colitis. The infection results following a disturbance in the normal intestinal flora following antibiotic therapy.

History-An anaerobic organism isolated and cultured with great difficulty in 1935 named Bacillus difficilis(now renamed Clostridium difficile) forms the most common cause of nosocomial diarrhoea[1]. Antibiotic-associated colitis occurs as an off-shoot of use of antibiotics and is noted specially in surgical patients. This was recognized in 1970s. A prospective study carried out by Tedesco and his colleagues in 1974 on 200 consecutive patients receiving clindamycin showed occurrence of diarrhoea in 41 patients. 20 (10%) of them who received clindamycin exhibited pseudo-membranous colitis[2]. Three years later Bartlett and colleagues found antibiotic-associated pseudo-membranous colitis to be due to a toxin-producing clostridium[3]. Since then C difficile has been the most commonly recognized microbial cause of nosocomial diarrhoea.

Aetiology-Clostridium difficile is a rod-shaped, gram-positive, anaerobic, spore-forming and cytotoxin producing, bacterium and is commonly found in hospital wards. Transmission occurs primarily in hospitals where the patient has been exposed to antimicrobial agents and to an environment contaminated by C difficile spores. The spores persist in the environment for prolonged periods. It happens to be the only anaerobe posing such a threat by producing toxin in the colon. Prolonged stay in hospital forms a major risk factor. It is acquired by the feco-oral route. It colonizes the human intestinal tract and multiplies after the resident flora has been altered by antibiotic agents An alteration in the normal colonic bacterial flora and impaired host immune response, facilitate the proliferation of the organism. There is an increase in incidence of C difficile-associated disease in US, Canada and Europe in the recent years due to emergence of an epidemic strain with increased virulence, antibiotic resistance or both. The hyper-virulent strain having a high concentrations of both A and B toxins has emerged to cause epidemics. A nation-wide-Swedish study revealed an increased mortality after the age of 60 years in C difficile-associated diarrhoea[4]. The risk factors were age over 65 years and receipt of fluroquinolones in the cases reported from Quebec, Canada [5]. There were many deaths from C difficile-associated disease in Pittsburgh, US. It was noted following fluoroquinolone use and it required colectomy in many cases [6].The increase appears to be due to emergence of a new strain of C difficile. In 187 C. difficile isolates collected from eight outbreaks at US health care facilities occurring between 2000 and 2003, a previously uncommon strain of C difficile with variations in toxin genes that has been more resistant to fluoroquinolones was encountered[7]. The strain belonged to toxinotype III and was positive for binary toxin.Loo et al in another microbial analysis with C difficile associated enteritis in 1703 patients at 12 hospitals in Quebec, Canada noted in 2004 that most strains to be resistant to fluoroquinolones and most of them had a binary toxin[8]. There was a very high incidence and mortality associated with increasing age. These data have proved that more virulent strains of C difficile are responsible for epidemics in selected locations. They are responsible for more severe disease, often associated with complications necessitating colectomy, and death.

Pathogenesis-C difficile is usually hospital-acquired. The

infection gets established when antibiotic therapy disrupts the normal colonic bacterial flora. The condition can develop in debilitated patients who have not received antibiotic therapy. Only about 3% of healthy adults and up to 20-40% of elderly persons may carry C difficile and remain asymptomatic carriers [9]. They act as a reservoir for infection. In healthy persons the organism remains in a metabolically inactive spore form and its colonization is not ordinarily harmful. The disturbance in the intestinal flora by the antibiotic or surgical interference facilitates its conversion to vegetative forms that replicate and produce toxins. Exposure to antibiotics is the chief precipitant of C difficile-associated diseases. Though any antibiotic with an antibacterial spectrum can result in severe intestinal disorder, the most commonly implicated antibiotics are clindamyin, cephalosporins and fluoroquinolones that disrupt the normal colonic bacterial flora[3,5]. There are many strains of C difficile with different pathogenic potentials. The virulence of the organisms is due to the two exotoxins (A and B) that are cytotoxic and inflammatory and they are produced by most pathogenic strains. These toxins are transcribed from a pathogenicity locus that comprises five genes: two toxin gene tcdA (toxin A) and tcdB (toxin B) and three regulatory genes, one of which (tcdC) encodes a putative negative regulator of toxin transcription[10]. These toxins bind to the receptors on the surface of the intestinal epithelial cells and get internalized and disrupt the cells significantly by uridine 5'-diphosphate glucose dependent glucosylation of rho proteins[11]. A binary toxin elaborated by C difficile encoded by two chromosomal genes cdtA and cdtB mediate cell-surface binding and disrupt the assembly of actin-filaments and result in cell death[12]. A hypervirulent strain having a mutation in tcdC is associated with high concentration of A and B toxins, and this strain was responsible for epidemics in USA, Canada, Europe and Japan[13]. TedC protein appears to inhibit toxin transcription during the early. exponential-growth phase of the bacterial life cycle, however it is intriguing why some persons carry them without any clinical manifestations. There are also toxin-negative organisms that do not produce any disease. Recent out breaks in US and Europe were due to a highly virulent, quinolone-resistant strain, PCR ribotype 027 (B1). It was capable of producing toxin 20 times more powerful that produced by A and B strains[14].

Pathology-Initially the infection is associated with focal areas of inflammation with oedema and erythema in the descending colon. It progresses with appearance of creamy-white adherent plaques on inflamed intact colonic mucosa without ulceration (pseudo-membrane). Pseudomembranes comprise of polymorphs, inflammatory cells, fibrin and debris, and may coalesce to obscure mucosa. There is secretory diarrhoea. The bowel wall gets thickened. There can be toxic megacolon and perforation.

Clinical features-The infection commonly develops in elderly, and frail patients often ailing with other co-morbid diseases in the hospital. These patients exhibit symptoms in the first week of receiving antibiotics. Though all antibiotics have the potential to cause C difficile associated disease, some antibiotics such as Clindmycin, second/third generation cephalosporins, amoxicillin/clavulanate and quinolones. However the development of the condition may be delayed up to 6 weeks after completion of therapy. The therapy would have been stopped by the time the manifestation become apparent. Apart from prior antibiotic therapy, prolonged hospital admission, nasogastric feeding, immunosuppression, age and chronic medical conditions form other factors that are associated with C difficile-associated disease (CDAD).The manifestations begin insidiously. The patients exhibit lower abdominal pain, low-grade fever and frequent passage of profuse, watery stools. Often they complain abdominal cramps. Severe colitis may result in small bowel ileus, toxic dilatation of colon (megacolon), perforation, and progressive multi-organ failure. Severe cases are associated with diarrhoea with 15-20 stools per day. Blood in the stools is unusual. Systemic toxicity is manifested with abdominal cramps, fever, and tachycardia. Ileus or megacolon may be heralded by cessation of diarrhoea [15].

Diagnosis-Colitis has to be suspected in any patient who is receiving antibiotic or has received antibiotics recently, when they have presented with diarrhoea. There is leucocytosis, hypoalbuminaemia, and high serum concentration of C-reactive protein. Leucocytosis may precede signs of colitis[16]. Radiologic imaging of abdomen may reveal dilated small intestine and colon without any free air. Sigmoidoscopy reveals erythema of the rectum and colon, and presence of raised yellow plaques or an adherent pseudo-membrane. Presence of pseudomembrane is pathognomonic. However its absence does not exclude the diagnosis as they are absent in mild cases and in patients with concomitant inflammatory bowel disease. Biopsy of the area has to be done for histopathologic study.Severe Cl. dificile infection includes pseudomembranous colitis, a marked peripheral leucocytosis, acute renal failure and hypotension. C. difficile organisms may be isolated by anaerobic stool culture. The positivity is higher in those exhibiting pseudo-membranous colitis compared to those having antibiotic-associated diarrhoea. The test though highly sensitivie, is non-specific due to the existence of non-toxigenic strains of C difficile that may colonize the bowel in hospitalised patients. Cell cytotoxicity bioassay helps in isolation of toxins A and B. Cytotoxic bioassay is performed by inoculating stool with cultured cells. The cytopathic effect is abolished by neutralising antibodies to C difficile toxin. This test is highly sensitive and specific. However its utility is limited by expense and the time needed to perform the assay (3 days)[14]. Rapid enzyme immunoassay (RIA) is fast (1 hour) and cheaper to detect toxin A or B or both. However the test has a low sensitivity.

Prognosis-The mortality in Cl difficile-associated disease (CDAD) varies from 5 to 10 percent. To this number the co-morbid conditions in elderly also contribute. Many patients who have received treatment successfully may exhibit recurrence of disease, This is because the administration either of metronidazole or vancomycin impairs resistance to colonization, and facilitate recurrent infection. It is commonly noted 4 weeks after completion of treatment.

Management - The administration of the offending antibiotic should be stopped immediately following development of diarrhoea. This will facilitate the normal bowel microflora to restore itself. The treatment may be changed to agents with a lower risk of inducing C difficile. Administration of corticosteroids, and other immunosuppressive agents and proton pump inhibitor (PPI) should be discontinued. The patient has to be isolated. The hydration of the patient has to be maintained by administration of intravenous fluids.The patients who are severely ill, and those exhibiting ileus, colonic dilatation or pseudo-membranous colitis need antimicrobial therapy. Of which metronidazole and vancomycin are widely used. The patients must receive them orally. Metronidazole is selected for initial treatment and it has to be given in a dose of 400 mg for seven to ten days. If the response is not satisfactory, and in more severe cases vancomycin 125 mg six-hourly has to be given for seven to ten days. Higher cure rates are seen with vancomycin in those with severe cases. Vancomycin is the first line treatment in patients with severe CDAD. Vancomycin has to be recommended when patients on metronidazole fail to show improvement within 72 hours[17]. Severe cases of CDAD require aggressive treatment with Vancomycin. It must be noted that IV vancomycin is not secreted into the lumen of the bowel. Some patients may benefit with intravenous metronidazole or vancomycin enema[18]. Generally these agents control the manifestations after 2-3 days. Recurrence of disease necessitates administration of metronidazole or vancomycin for 10 to 14 days. It must be noted that substantially higher failure rates are encountered in the recent years for metronidazole therapy[19].In a recent study comparing vancomycin (125 mg four times a day) with metronidazole (250 mg four times a day) for the treatment of Clostridium difficile-associated diarrhoea stratified by disease severity, Zar and colleagues found both agents showing similar efficacy in mild infection. However, the response rate with Vancomycin (98%) was greater than that with metronidazole

(90%). Vancomycin was significantly more effective in severe infection[20]. Metronidazole is recommended for mild infection due to its lower cost and concerns about the proliferation of vancomycin-resistant nosocomial bacteria. Vancomycin is to be used as first-line agent in patients with severe infection because of more prompt symptom resolution and a significantly lower risk of treatment failure[21]. Oral vancomycin may not be suitable for some patients with severe or fulminant infection due to coexistent ileus or toxic megacolon. In such situations metronidazole has to be given in a dose of 500 mg four times a day with supplementation of vancomcin[21].20,000 units of Bacitracin orally 6-hourly and 300 mg of Fusidic acid orally every 6 hours are other drugs that can be utilized in the management for a week. Probiotic, Saccharomyces boulardii 500 mg twice daily may be administered as adjunct to antimicrobials. However it is not recommended in immunosuppressed patients or those with central intravenous lines as there is likelihood of occurrence of fungaemia[18]. In a small number of cases who are therapy-resistant, administration of a filtrate of stools from a healthy family member, either through a nasogastric tube or at colonoscopy may help in reconstitution of faecal flora[18]. However this procedure is not popular due to practical and aesthetic reasons. Fulminant cases are treated with intravenous immunoglobulin, and some cases may require urgent colectomy.

Prevention-It is necessary to maintain proper hygiene of the ward. Periodic disinfection of the hospital environment, and cleaning with dilute bleach has to be carried out to eliminate C difficile spores. Proper washing of hands with soap and water is stressed. Health care workers should wear gloves and gowns when entering the room of patient. Judicious use of antibiotics is an important way to reduce the incidence of C difficile infection. The use of the epidemiologically implicated antibiotics such as clindamycin, second and third generation cephalosporins or fluoroquinolones are to be restricted in surgical cases. The patients have to be isolated and treated. The administration of probiotics in hospitalized patients requiring antibiotics significantly brings down subsequent incidence of antibiotic associated diarrhoea[22]. Strict isolation of patients, barrier nursing, good hand washing procedures with soap and water, and environmental decontamination with sodium hypochlorite solution to kill the spores on the surfaces, help in achieving secondary prevention of transmission of C difficile and its spores.The recent surge in outbreaks shows that known pathogens can alter their behaviour and pose new threat with increased virulence, antimicrobial resistance or both. Even after seven decades of its isolation C difficile posing difficulty in containment of its growth and spread.

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Commentary

Assisted Reproductive Technology and Anesthetic considerations - review of literature

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The first successful live birth following in-vitro fertilization (IVF) of a human oocyte was performed in 1978 by Steptoe and Edwards with the birth of Lousie Brown, the first test tube baby. Assisted Reproductive Technology (ART) has gradually evolved into more sophisticated with advancement and better outcome. Similarly the related anaesthetic techniques as well. The anesthesiologist may be involved in many aspects of the patient's treatment, which may be complex and needs cautious perioperative management. IVF is a four stage procedure – ovarian stimulation and monitoring, oocyte retrieval, fertilization and embryo transfer. Egg retrieval can be accomplished laparoscopically or ultrasound guided vaginal retrieval.

Need of anesthesiologist- Majority of the patients are young and healthy but exhibit stress, anxiety and other psychological disorders associated with infertility. It is particularly important for the anesthesiologist to understand the patient's anxieties and take suitable measures to allay it. The serum hyperprolactinaemic response to stress is well established[1]. 50-fold transient increase in serum prolactin levels during oocyte retrieval for in-vitro fertilization has been reported under general anaesthesia which may influence the outcome of IVF [2,3,4,5]. The need of repeated attempts of IVF before success is achieved, also mandates taking care of psychological stress and alleviating it. The IVF procedures are also associated with pain and hence the need of minimization of pain is a major consideration[6]. The cooperation of patient is required during IVF procedure like oocyte retrieval, which some time mandates the need of anaesthesia even.

Anaesthetic considerations- For ART procedures, the factors to be taken under considerations includes the technique of anaesthesia, pneumoperitoneum (if laparoscopy required), and the effects of anaesthetic agents on fertilization and cell cleavage. The length of exposure to drugs is also important. Now a days, the ART procedures are being accomplished as 'Day care' cases and the basic principles of 'Ambulatory anaesthesia' needs to be followed. Laparoscopic oocyte retrieval has now largely been superseded by ultrasound-guided transvaginal oocyte retrieval[5].

Effect of anaesthetic agents on reproductive techniques- Controversy exists regarding the effects of anesthetic drugs administered during transvaginal puncture procedures for oocyte retrieval on conception rates[7]. Anesthetics have been detected in follicular fluid, and studies suggest that these drugs may adversely affect oocyte fertilization and embryonic development. It has also been confirmed that the use of general anaesthesia with nitrous oxide for oocyte retrieval has an adverse outcome on the outcome of IVF; the deleterious effect manifests itself only after embryo transfer and leads to lower pregnancy and delivery rates[8,9]. Exposure to pneumoperitoneum with carbon-di-oxide adversely affects oocyte quality and in combination with exposure to general anaesthesia with nitrous oxide appear to affect fertilization and cleavage in vitro[7]. However, Rosen et al failed to demonstrate an adverse effect of nitrous oxide on fertilization or pregnancy rates when administered during an isoflurane-based general anesthetic technique[10]. Anesthetic drugs have been detected in follicular fluid, and a longer period of exposure in the general anesthesia group may have enhanced the deleterious effects of these drugs on the oocyte and/or follicular structures, thereby interfering with the reproductive process [11,12,13,14]. Halogenated agents have been associated with reduced reproductive success in clinical practice and must therefore be used with caution[7,15]. Opioids, and especially fentanyl and

remifentanil, do not seem to affect reproductive success.

Exposure to high concentrations of different local anesthetics adversely affects fertilization and embryonic development[16]. However, given that much lower concentrations are achieved clinically and that oocytes are washed after retrieval, the clinical effects of using local anesthetics should be limited and probably no adverse effects should occur.

Pain in IVF-Oocyte retrieval is a fundamental step but reported to be the most painful component of the IVF procedure[17,18,19]. Although less invasive than the laparoscopic approach, transvaginal oocyte retrieval still remains a painful procedure[20,21]. The pain experienced during oocyte aspiration is caused by the passage of the needle through the vaginal wall and by mechanical stimulation of the ovary[6,22]. The pain is often described as similar to intensive menstrual pain and is intermittent rather than continuous. Factors that may influence the pain are the number of follicles, duration of the oocyte retrieval procedure, the position and mobility of the ovaries[22]. Multiple-follicle aspiration would entail a lengthier procedure, which could affect pain scores when compared with single-follicle aspiration[23]. A good analgesic method for oocyte retrieval has to give satisfactory pain relief with rapid onset, rapid recovery, ease of administration and monitoring[17,18,19]. In addition, the analgesic method must have no toxic effects on the oocytes and embryos since many agents have been detected in the follicular fluid shortly after administration[24,25,26,27.]

For alleviating pain of IVF, opioids and benzodiazepines has been used, however, many of these agents have been detected in the follicular fluid, albeit clear evidence to indicate negative effects on oocytes, oocyte differentiation, implantation or pregnancy rate is sparse. More and more patients, however, are requesting sedation or anaesthesia for ultrasound-guided oocyte retrieval. It is also important to use anaesthetic agents that are safe, has no toxic effects on the oocytes and ensures the highest fertilization and pregnancy rates[17,28].

IVF Anaesthesia techniques-Transvaginal ultrasound-guided oocyte retrieval as a part of in vitro fertilization is the most common method of oocyte retrieval and is a relatively short (20±30 minutes) outpatient procedure[19,22,28]. As such, it requires an anesthetic technique that works quickly and effectively during the procedure but also allows for a rapid recovery with minimal side effects. Traditional analgesic methods used for transvaginal oocyte retrieval include local injection as a paracervical block, conscious sedation using various pharmacological agents, epidural block, subarachnoid block, general anaesthesia, or in some cases no analgesic at all[6,23,21,29,30,31-36]. The principle of a balanced multimodal approach to analgesia has been shown to be effective at treating pain in other clinical settings such as cancer[23]. The end point of in vitro fertilization procedures is ultimately the rate of successful pregnancies. Viscomi et al found no difference in fertilization and pregnancy rates between intravenous sedation and spinal anesthesia[37]. Rosenblatt et al noted that the addition of propofol to intravenous sedation for egg retrieval did not affect pregnancy and implantation rates[38]. Gonen et al did find that general anesthesia with a number of drugs was associated with decreased pregnancy rates when compared with epidural anesthesia[39].In a systemic review by Stener-Victorin for methods of conscious sedation during assisted reproduction techniques, concluded that no single technique may be regarded as superior to other for pain relief during oocyte retrieval[6]. Similarly, in an another Cochrane review by Kwan et al and found, on analysis of studies regarding conscious sedation and other alternate techniques of pain relief, that no single method or delivery system appeared superior for pregnancy rates and pain relief[23]. Various methods for analgesia reviewed were sedation with midazolam, ketamine, fentanyl, alfentanyl or electro acupuncture along with paracervical block, intramuscular pethidine and/or piroxicam and general anaesthesia with intravenous fentanyl and propofol. It was concluded that there is insufficient evidence to determine the best method of pain relief for oocyte retrieval .Monitored anesthesia care or intravenous sedation with fentanyl and midazolam was used for egg retrieval, but patient

discomfort and motion during the procedure led to the use of other anesthetic techniques[28]. Spinal anesthesia has been used because it provides excellent surgical anesthesia with minimal use of intravenous medication. An alternate technique is intravenous general anesthesia with fentanyl, midazolam, and propofol. General anaesthesia will abolish the issue of pain during oocyte retrieval but is likely to have resource implications. In choosing appropriate regimens for sedation/analgesia for oocyte retrieval, a balance may need to be struck between safety and efficacy. The ideal regimen would reduce pain to a tolerable level in all patients without the risk of adverse respiratory or cardiovascular events[23]. Cons-cious sedation allows patient co-operation to be maintained and the procedure to be conveniently performed in the outpatient setting. This remains the most commonly used method of providing analgesia and anaesthesia during transvaginal oocyte retrieval and is used in 84% of IVF clinics in the UK and 95% of IVF centers in the USA. By comparison, 16% of UK clinics and about 50% of clinics in Germany use general anaesthesia for IVF procedures[23].

General anaesthesia-Wilhelm et al compared the outcome of assisted reproductive technology procedures in 251 women who undergo monitored anaesthesia care with remifentanil versus general anesthesia (alfentanyl, propofol, isoflurane, nitrous oxide)[7]. They concluded that the ppregnancy rates in women undergoing transvaginal oocyte retrieval for assisted reproductive technologies were significantly higher with a remifentanil-based MAC technique than with a balanced general anesthetic technique involving nitrous oxide.

Regional / Local anaesthesia- In a study by Zaccabri et al vaginal application of EMLA was compared with paracervical block for Oocyte Retrieval. Pain was evaluated by visual analog score (VAS) and the outcome was that no one protocol satisfied the patients; authors suggested improvement of premedication strategies. Intervention such as paracervical block when added to the opiate conferred further benefit[23]. Paracervical block induces good analgesia, which is enhanced further by intravenous sedation[6]. In study of the intraoperative pain scores associated with intravenous fentanyl plus paracervical block versus electro-acupuncture plus paracervical block favored intravenous fentanyl for IVF[23]. Paracervical block with bupivacaine was superior to paracervical block with saline or no treatment and oral diazepam, and intravenous alfentanyl in combination with paracervical block was superior to electro-acupuncture in combination with paracervical block[6,24]. Regarding abdominal pain 60–120 min after oocyte retrieval, electro-acupuncture was superior to intravenous alfentanyl, in combination with both paracervical block. Randomized, controlled trials suggest that pain relief is superior when a paracervical block is used in addition to sedation, as compared with sedation alone[17,2]. It has also been shown that patients who received only paracervical block during oocyte collection experie-nced 2.5 times higher levels of vaginal and abdominal pain than those who received both paracervical block and conscious sedation[17]. A new technique, pre-ovarian block (POB), has been introduced by one of the authors of this study (I.Ek)[17]. The local anaesthetic is infiltrated under ultrasound guidance in the vaginal wall and between the vaginal wall and the peritoneal surface near the ovary. The follicle aspiration needle is then inserted in exactly the same location as the deposited lidocaine. Cerne et al studied pre-ovarian block versus paracervical block for oocyte retrieval in prospective, randomized, multicentre study including183 patients[17]. All participants in both the groups received alfentanyl 0.25 – 0.5 mg intravenously prior to procedure. Rescue analgesia was provided with bolus alfentanyl 0.25 mg. All patients received rectal paracetamol 1 g preoperatively. Anxiolysis was given by oral flunitrazepam 0.5 mg or 2.5 mg of midazolam. They concluded that both techniques provided comparable pain relief and both pre-ovarian and paracervical block in combination with intravenous alfentanyl may be considered safe methods with rapid onset, recovery and ease of administration. A paracervical block (PCB), in combination with different sedative pre-

medications with or without fast-acting opiates, has been reported to give acceptable pain relief during oocyte aspiration in several studies[22]. Hung et al concluded from his prospective, randomized, double blind and placebo controlled study to assess the efficacy of paracervical block in the pain relief during egg collection in IVF that paracervical block with lignocaine should be used in conjunction with iv sedation / analgesia (50 mg pethidine and 25 mg promethazine given 1 hour prior and 25 mg pethidine and 5 mg diazepam given 5-10 minutes prior to procedure) during egg collection performed through the transvaginal route under ultrasound guidance to reduce the pain of the procedure[40].A possible risk associated with paracervical block is the potential toxicity of absorbed lidocaine[24,41]. In human use, however, there is no evidence of adverse events associated with lidocaine[17]. No adverse effects on fertilization, cleavage or pregnancy rates were shown using paracervical block[24]. Paracervical block with different doses of lidocaine has been studied, and no differences were found in pain levels during oocyte retrieval when 50, 100 or 200 mg was used[35,36]. Thus, the lowest dose has been recommended. Lidocaine is a well-documented local anaesthetic often used for paracervical block (PCB) in pregnant women. It thus seems that the concentration of lidocaine found in the follicular fluid after PCB with 50 mg lidocaine does not negatively affect fertilization of the human oocyte or early cleavage of the human embryo[24]. Intrathecal fentanyl, in combination with local anesthetics (lidocaine), can improve the quality and prolong the duration of intraoperative analgesia[28]. Epidural anaesthesia, the most popular of the obstetric anaesthetic techniques offers no obvious advantages over the IV sedation or the other methods for Oocyte Retrieval nor does it improve the treatment outcome.

Propofol-Propofol has been a promising alternative for Thiopental for short surgical procedures and has been tried for oocyte retrieval. No significant differences exist between the two drugs as regards the fertilization rate, cleavage rate, pregnancy rate, implantation and abortion rate[27]. However propofol should be used with caution, despite its advantages. Propofol has been suspected of damaging oocytes. Concentrations of propofol have been shown to increase in follicular fluid with time, during oocyte retrieval[26]. A study was designed to assess whether exposure to increasing concentrations of propofol has any measurable effect on in-vitro fertilization, cleavage and embryo development. There was an increase in the concentration from the first to the last follicle, but no difference was found in the ratio of mature to immature oocytes. Nor were any differences found in fertilization, cleavage and embryo cell number[27]. It was concluded that the time elapsed between retrieval of the first and last oocyte does not affect oocyte quality. However it is advisable that the IVF procedure should be kept as short as possible in order to limit the accumulation of the anaesthetic in the follicular fluids.

Sedation and monitored anaesthesia care (MAC)- Concerns regarding the potentially deleterious effects of anesthetic drugs have led to the use of anesthetic techniques that minimize exposure[7]. Increasingly, these procedures are performed with sedative and/or analgesic drugs as part of a monitored anesthesia care (MAC) technique. Trout SW strongly advocates conscious sedation (with opioids and benzodiazepines) for IVF[19]. Several other studies demonstrated higher pregnancy rates in women who underwent oocyte retrieval under MAC with Remifentanil infusion than with GA. Midazolam/Remifentanil regimen was evaluated to be as effective and safe as propofol/ fentanyl regimen. Several opioids, such as, pethidine, morphine, fentanyl and remifentanil, have been used as a part of conscious sedation and monitored anaesthesia care and have been effective at reducing perception of pain.Lok HI et al in his prospective randomized trial comprising 106 patients comparing patient controlled sedation using propofol (10 mg/ mL) and alfentanyl (50 mcg/mL) (bolus dose of 1 mL and effective lock out time of 18 sec) and physician administered sedation using diazepam (0.1 mg/kg) and pethidine (0.5 mg/kg) (administered intravenously 5-10 minutes prior to procedure, and additional doses of pethidine 0.5 mg/kg were given when required) during

transvaginal ultrasound guided oocyte retrieval[32]. They concluded that though patient controlled sedation provided less analgesia than physician contrrolled sedation but it is safe, satisfactory and accepted by patients. The combination of midazolam and ketamine was compared with general anaesthesia with propofol and isoflurane[42]. No intraoperative pain was remembered in either group. Hein et al. presented data on two different MAC techniques that suggested that the pregnancy rate was higher when a combination of midazolam, fentanyl, and propofol (vs. fentanyl, ketamine, and methohexital) was used[43]. Propofol was also used in a more recent study at two different dose levels to achieve either general anesthesia or intravenous sedation; and no difference was found in the pregnancy outcome rates[7]. In a comparison between propofol-based general anesthesia and paracervical local anesthetic blockade, Christiaens et al found no differences between the fertilization rates or embryo cleavage characteristics[44]. These investigators also reported that the initial implantation rate after propofol anesthesia (13.4%) was similar to the rate in the local anesthetic group (18.6%)[7]. The results of a retrospective chart review also found no evidence that the administration of propofol during aspiration of ovarian follicles had a negative impact on oocyte cumulative embryo scores, implantation, or pregnancy rates[44]. Remifentanil, which is a rapid and ultra-short acting opioid analgesic, also has been successfully used for ultrasonic- guided oocyte retrieval procedures as part of a MAC technique[45,46,47]. The present retrospective study compared pregnancy outcome of ART procedures in women exposed to either general anesthesia or MAC with remifentanil[7]. This retrospective study suggests that in women undergoing transvaginal ultrasound-guided oocyte retrieval procedures, the likelihood of a successful pregnancy is higher with a remifentanil-based MAC technique than with a "balanced" general anesthetic technique. These findings are supported by a preliminary report by Toon et al suggesting an increased pregnancy rate in women having spinal compared with general anesthesia for oocyte retrieval[48]. Interestingly, use of electro-acupuncture in combination with a paracervical block for oocyte aspiration was judged a good alternative to an opioid-based MAC technique, with an even higher pregnancy rate[49].

Patient controlled analgesia (PCA)-PCA may facilitate an individualized approach and, by allowing women a degree of control over their drug administration, lead to higher levels of patient satisfaction[50]. The effect of i.v. PCA was evaluated in two studies and was considered to be as effective as physician-controlled techniques[31,32]. Bhattacharya et al performed the study to evaluate the efficacy of patient controlled analgesia during oocyte recovery. They premedicated their patients with 4 mg midazolam and 25 mcg of fentanyl. Maintenance bolus doses were then administered by the clinician or by the patient herself using patient controlled analgesia pump (10 mcg fentanyl bolus with 1 min lock out). They concluded patient controlled analgesia fentanyl is an effective alternative to physician administered techniques in terms of patient comfort and satisfaction. Despite high satisfaction rates, many women still feel the need for more analgesia during the procedure[31].However, since physician controlled sedation demands higher doses of analgesics and many drugs have been found in the follicular fluid shortly after i.v. injection, it is questionable whether this method is optimal in the present situation[6]. Patients also reported high levels of satisfaction with intravenous opiates administered by a physician or the patient[31,32].

Electro-acupuncture (EA)-Recently, electro-acupuncture, activates the endogenous opioid system responsible for pain has been reported to decrease pain during oocyte retrieval and have fewer negative side effects[18,49,51,52]. Acupuncture is a pain-relieving method that activates endogenous pain-inhibiting systems such as the spinal/ segmental gate mechanism and the endogenous opioid systems[52]. Electro-acupressure was compared with alfentanyl infusion and was found to be a good alternative for conventional anaesthesia. Humaidan et al compared the role of electro-acupuncture as an alternative to conventional analgesic method in an prospective randomized study in 200 women[53]. Both the groups received paracervical block. The

conventional analgesic method used was benzodiazepine premedication, alfentanyl 0.25 mg boluses. Rescue analgesia was provided with intravenous alfentanyl in both the groups. They found significant difference in intraoperative pain. More pain in electro-acupuncture group was attributed probably to administration of premedication in conventional analgesic group. The procedure was well tolerated in both the groups. Gejervall et al compared the pain reliving effect and postoperative well being between electro-acupuncture and conventional analgesia in an randomized study in 160 females for oocyte retrival[22]. Paracervical block was given in both the groups. Conventional analgesia was provided with intravenous alfentanyl along with 0.5 mg flunitrazapem and 1 g paracetamol premedication. Rescue analgesia was provided with alfentanyl or notrox. They concluded that electro-acupuncture cannot be generally recommended as a pain reliving method at oocyte aspiration but might be an alternative for women desiring a non-pharmacological method. An advantage of electro-acupuncture is less postoperative tiredness and confusion compared with conventional analgesia.Stener-Victorin et al evaluated the efficacy of electro-acupuncture as peroperative analgesic method during IVF in two different syudies[18,49]. The electro-acupuncture was comp-ared with alfentanyl. Both groups received paracervical block as well. The alfentanyl group received 0.5 mg alfentanyl and 0.25 mg atropine intrave-nously directly before a paracervical block was placed and oocyte aspiration began. Rescue analgesia was boluses of alfentanyl. They concluded that analgesic effects produced by electro-acupuncture are as good as those produced by conventional analgesics, and the use of opiate analgesics with electro-acupuncture is lower than when conventional analgesics alone are used. But women experience less abdominal pain, less nausea and less stress at 2 h after oocyte aspiration, and also use less opiate analgesics than when conventional analgesics alone are used.

Conclusion-Variety of anaesthetic techniques and analgesic methods has been used but no definite conclusion has yet been arrived regarding the technique of choice for IVF. No method could be considered as superior to other technique if basic concepts pertaining to IVF are taken care. Conscious sedation is suitable for cooperative females. In addition to conscious sedation and analgesia, many methods of pain relief during oocyte recovery are currently in use. In case general anaesthesia is required, the anaesthetic drugs should be used cautiously and efforts should be made to reduce the anaesthetic duration. The preferred modality of peri-operative care should be invidualized as per the requirement of the patient.

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Vision 2020 - The Right to Sight

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The suffering and anguish blindness brings has been documented throughout the history. Curing blindness is a not a recent phenomenon however concept of avoidable blindness came into forefront in the prevention of blindness control programme more recently. Avoidable blindness has been defined as blindness that could reasonable be prevented or cured within the limits of resources that are likely to be made available. Approximately 75-85% of all blindness is considered to be avoidable. Blindness is estimated to cost $25 billion annually. Though blindness afflicts all nations, it is most vicious in the developing world. Blindness in developing countries is generally associated with poverty and ignorance and is most commonly found in rural often remote and underdeveloped areas as well as in the urban slums. 'Sight' is a fundamental right of all human being to appreciate unlimited blessings of mother-nature and it needs to prevented from getting deteriorated; corrected and/or restored by all means and strategies.

Definition-Blindness is defined in different ways by different people. To a layman, blindness conjures up images of a person who is completely blind with no perception of light. However, in ophthalmic practices not only these cases of 'absolute blindness' but also those with severe impaired VISION are also labeled as blind. WHO has defined blindness as visual acuity of less than 3/60 or a corresponding visual field loss to less than 10 degrees in the better eye with best possible correction or inability to count fingers at a distance of 3 meters.[1] National Programme for Control of Blindness [NPCB] in India has defined blindness with visual acuity of less than 6/60 or restriction of field VISION to less than 10 degree in the better eye with best possible correction [presenting VISION] or inability to count fingers at 6 meters [20 feet]. Economic blindness refers to that level of VISION, which hampers the earning potential of an individual whereas Social blindness refers to further deterioration in VISION such that an individual is not able to undertake activities for daily sustenance and is unable to interact properly with others in his/her own family and community. Classification of blindness as per WHO and NPCB criteria is shown in Table 1.[2]

The WHO study group emphasized that each country must define blindness in relation to its own social and economic conditions, keeping the categories of visual impairment in mind. The blindness definition in India has been more liberal than their international partners so as to provide rehabilitation services to these individual in the country whose VISION did not permit them to earn a livelihood. However, for all international comparisons, standard case definitions should be adhered to i.e. cut off point for international comparison was placed at 3/60 [inability to count fingers at a distance of 3 meters]. The term visual impairment includes cases with blindness as well as low VISION.

Low VISION presents with all three of the following characteristics:

- Impairment of visual functioning even after treatment and/or standard refractive correction.[3]
- Visual acuity ranging from light perception to <6/18 or a visual field smaller than 20 degrees in the better eye with best possible correction.[1]
- The person uses, or is potentially able to use, VISION for the planning and/or execution of a task.[4]

Global- Every five seconds one person in the world goes blind; every minute, one child goes blind.[5] The first global analysis of data on blindness by WHO indicated that in 1975 there were 28 million blind people i.e. visual acuity less than 3/60 in the better eye with best correction. Estimates in 1990 showed that this figure would continue to increase, from 38 million in 1990

to 45 million in 2000. Projections based on the global population increase and ageing, predicted 58 million blind in 2010 and 75 million by 2020 unless special efforts are taken to arrest and reverse the trend. Of the estimated 45 million blind people in 2000, approximately 60% of blindness due to cataract and refractive errors [treatable]; 15% was due to trachoma, vitamin A deficiency and onchocerciasis (Africa) [preventable]; another 15% of blindness was due to diabetic retinopathy and glaucoma [partly preventable, although more difficult]; and the other 10% was attributable to age-related macular degeneration and other diseases [more research required for best treatment].[6] According to WHO criteria, there were estimated 6.7 million blind in India as of 2002.[1]

South East Asia-The 11-countries [Bangladesh, Bhutan, India, Indonesia, Maldives, Myanmar, Nepal, Srilanka, DPR Korea, Thailand, Timor leste] in this WHO region constitutes 25% of worlds population, 40% of world's poor, 33% of worlds blind, 50% of world's childhood blindness, 60% of world's cataract backlog cases and highest number of blind persons among WHO regions. The prevalence of blindness in the region is around 0.8% [range vary from 0.3% for Thailand to 1.5% for Indonesia].[7]

India-has a population of more than one billion and the first survey undertaken by Indian Council of Medical Research [ICMR] in 1974 indicated a prevalence of 1.38% of general population [visual acuity <6/60]. In the second survey [1986-89] sponsored by GOI-WHO, the prevalence rate increased to 1.49% [VA <6/60]. As per available information from various studies, there is an estimated 12 million bilaterally blind persons in India with VA <6/60 in the better eye of which nearly 07 million are with visual acuity [VA] <3/60 in the better eye. Recent survey [1999-2001] in 15 districts of the country indicated that 8.5% of 50+ population is blind [VA <6/60].

VISION 2020[8]-VISION 2020 may have different connotations in different settings and personnel choices. In USA, 20/20 stands for optimum eyesight and at the same time, it also denotes the year 2020 from planning and developmental perspective. The objective "VISION 2020" is that no one should be needlessly blind any longer by the year 2020. It is an initiative with a common objective, which will allow people cutting across nations to work in a focused and coordinated manner to help raise global awareness about blindness and mobilize additional resources to prevent or treat avoidable blindness. VISION 2020 will further develop and strengthen the primary health/eye care approach to problem of avoidable blindness. This will be done on the basis of the invaluable international and national experiences already gained through ongoing national programs. Finally, the initiatives will seek broad regional alliances and eventually a global partnership for eye care. These partnerships are indispensable in establishing worldwide the fundamental right "Right to Sight" and thus save future generations from the tragedy of needless blindness.

Global initiative - Many organizations have attempted to combat the problem of blindness in the past. However it was felt that there should be an umbrella under which all these organizations could be unified for effective output.[9] A joint initiative-eventually named VISION 2020: the Right to Sight was conceived by World Health Organization [WHO] and International Agency for Prevention of Blindness [IAPB] and its constituent members. It was enshrined to provide technical guidance and support to countries that adopt the agenda of strong partnership among ministry of health, national and international organizations involved in eye care, professional organizations, and civil society groups- brought together on a common platform in a national prevention of blindness programme.

The **mission** of VISION 2020 is to eliminate the main cause of avoidable blindness in order to give all people in the world, particularly the millions of needlessly blind, the right to sight.

The **goal** of VISION 2020 is to eliminate avoidable blindness by the year 2020. In long term, the initiative seeks to ensure best possible VISION for all people and thereby improve their quality of life. This goal is to be achieved through establishment of

sustainable, comprehensive eye-care system as an integral part of every national health system.

The **objectives** of VISION 2020 include raising the profile-among key audiences-of the causes of avoidable blindness and of the solutions that will help eliminate the problem; identify and secure the necessary resources around the world in order to provide an increase level of activity in prevention and treatment programme; and facilitate planning, development and implementation of the three elements of the VISION 2020 strategic plan by national programme.

Strategy of VISION 2020 is built upon a foundation of community participation, with three essential components or elements:

- Cost effective disease control interventions;
- Human resource development [training and motivation]
- Infrastructure development [facilities, appropriate technology, consumables and funds].

The guiding **principles** of VISION 2020 are:

- Integrated into existing health care system
- Sustainable in terms of money and other resources
- Equitable care and services available to all, not just the rich
- Excellence i.e. high standard of care through out.

National response - The Director General of WHO launched VISION 2020: the Right to Sight in Geneva on 18th Feb 1999 which was followed by series of advocacy workshops in South East Asia [WHO] region during September 1999 to Feb 2000. This lead to national and sub-national consultative workshops and processes during 2001-03 with formulation of National Plan of Action leading to reinforcement of commitment and collaboration of stakeholders wherein a road map for amelioration of blindness in the country was detailed. This included physical targets, strategies for strengthening human resource development, eye care infrastructure, advocacy, management information system, national activities, recommendations of national workshops for reduction of disease burden & primary eye care and other important milestones. Target diseases for VISION 2020: India includes cataract; childhood blindness; refractive errors and low VISION; corneal blindness, glaucoma; diabetic retinopathy and trachoma [focal].[10, 11] Inspite of various constraints and with reasonable success in controlling cataract-related blindness, other blinding conditions are increasingly and adequately being addressed in the XIth five-year plan period [2007-12] of National Programme for Control of Blindness, Government of India. Financial allocation has been increased tremendously to bring other blinding conditions in the forefront, ophthalmologist in public sector are being trained on these issues at various public and NGO institutions, Diabetic Retinopathy and Glaucoma screening & management is being addressed in this plan, low-VISION aids will be provided in selected medical colleges and Regional Institute of Ophthalmology [RIO], advocacy workshops are being held at national and regional level for orienting health personnel and stakeholders, newer strategies are being devised to enhance voluntary eye donation in the country through consultative processes, comprehensive evaluation of programme as well as IEC component under NPCB has been commissioned to determine the strengths and weakness of existing strategies/components/schemes/mechanism of disbursement of funds and to revamp information education and communication [IEC] component based on the input from these evaluation, involvement of other stakeholders like Integrated Child Development Scheme functionaries [Anganwadi workers etc] under Women and Child Ministry, Education department under Ministry of Human Resource Development [HRD], Panchyati Raj Institution [PRI] have been specifically roped into strengthen and increase the visibility of programme activities at grass-root level etc.

VISION 2020- India is a conglomeration of different NGOs working in eye care in the country and came into existence in May 2004 with its secretariat in New Delhi, India. The member organizations in VISION 2020 team has grown to 65 as of March 2008 and its founder member included:[12]

- International non-governmental organization [INGO]- Christoffel- Blindenmission, Germany; Sight Savers International, United Kingdom; ORBIS International, USA; Opera-tion Eye Sight Universal, Canada; Seva Foundation, USA
  Lion Clubs International Foundation, USA
- National non-governmental organization [NGO]-L.V Prasad Eye Institute, Andhra Pradesh; Aravind Eye Care System, Tamil Nadu
- National Governmental Organization [GO] - Dr. Rajendra Prasad Institute for Ophthalmic Sciences, AIIMS, New Delhi

The prime role played by VISION 2020: India is

- Supportive and participative in implementation of National plan of action of Government of India [GOI] especially in underserved areas;
- Advocacy through formulation of state level plan of actions and programme; organizing events like World Sight Day [2nd Thursday of October], Eye donation fortnight [23rd Aug to 8th Sep] in collaboration & financial assistance from GOI and building strong network of national NGOs;
- Information collection and dissemination: mapping of INGO for information of services and partnership; facilitating development of training modules, manuals, protocols, guidelines, resource material pertaining to strategic thrust area of VISION 2020 and making it available to eye care institutions; regular interface/ interactions amongst various stakeholders and keep them updated on all issues; holding national events and regional conferences with VISION 2020 themes every year.
- Resource management: mobilization of resources from members and new sources for carrying out programme activities
- Research and publication

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Table-1, Comparison of WHO and NPCB definitions[2]

WHO-ICD classification of visual impairment and blindness	Visual acuity	NPCB categorization of visual impairment and blindness
Low VISION		
Category [1]	<6/18-6/60 in better eye	Low VISION
Category [2]	<6/60-3/60 in better eye	Economic blindness
Blindness		
Category [3]	<3/60-1/60 in better eye	Social blindness
Category [4]	<1/60 in better eye-perception of light	
Category [5]	No perception of light	

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Nitrous oxide

Nitrous oxide is a relatively weak anaesthetic. A concentration of at least 50 per cent is required to produce worthwhile analgesia. For this reason, nitrous oxide is always mixed with oxygen instead of air. Two types of apparatus are used. The first mixes the two gases (supplied separately) before delivery to the patient. This apparatus is usually fixed permanently to the wall, and the concentration of nitrous oxide can be adjusted within the range of 0-50 per cent or 0-70 per cent (depending on national regulations). These upper limits ensure that patients will not lose consciousness and can never receive less oxygen than exists in room air (21 per cent). This type of apparatus is popular in Australasia. Being a wall fixture, it is not portable and so cannot be used for a home delivery. The other kind of apparatus which is commonly used to supply nitrous oxide is called 'Entonox'. In this case, a 50:50 mixture of nitrous oxide and oxygen is contained in a single cylinder . A special valve at the top of the cylinder reduces the pressure to safe levels (so there is absolutely no danger of being 'blown up'!). It is not possible to alter the concentration of nitrous oxide when using Entonox, but in practice, this does not seem to be important. One advantage of Entonox is that it is portable, and can therefore be used for home deliveries (in Britain, but not in Australia). Entonox is also used in many countries by paramedical personnel to provide pain relief at accident sites and in ambulances.

Like all drugs that enter the bloodstream, nitrous oxide is distributed throughout the body. It also passes very easily across the placenta and is distributed likewise throughout the baby's body. Unlike opioid drugs, however, nitrous oxide is excreted from the body very quickly - and entirely - by the lungs. It does not have to be broken down (or metabolised) first by the liver and so there are no 'by-products'. This rapid elimination of nitrous oxide also applies in the case of the baby: within five minutes of birth it cannot be detected in the baby's breath at all. Because of its rapid elimination, it doesn't really matter how long nitrous oxide is used; the gas does not 'build up' or accumulate to any degree whether it is used for five minutes or five hours.

Most large surveys have come to similar conclusions regarding the effectiveness of nitrous oxide in labour when it is used properly. Rather less than 50 per cent of women claim satisfactory relief: 20 per cent obtain some relief for some of the time, and approximately 30 per cent find it completely ineffective.

4

Effective Communication-Resident's Perspective

Commentary

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Communication is part of our normal relationship with other people. We are not only communicating with 'others' but also with 'ourselves' throughout the day. In our professional setting, we are involved in communicating with superior, colleagues, juniors, patients and their attendant. Our ability to influence others depend on our communication skills e.g. speaking, writing, listening, reading and reasoning.These skills are very important in health education especially while interacting with patients and their attendants. Studies have shown that at least 50% of patients leave the doctors' chamber not knowing what they have been told; 50% of psychosocial and psychiatric problems are missed by physicians due to lack of proper communication[1]; physician interrupt patients on an average of 18 seconds while patient is describing his/her presenting problems[2]; 54% of patients' problems and 45% of patient concerns are neither elicited by the physician nor disclosed by the patient[3]; and 71% of patients stated poor relationships as a reason for their malpractice claims [4] ; whereas 95 % of medico-legal cases occur due to a communication breakdown between the patient/ relatives and the doctor.[5] Research has consistently demonstrated that patients' understanding of their conditions and treatment is positively related to adherence[6], and that adherence, satisfaction, recall, and understanding are all related to the amount and type of information given[7] and patients who understand the purpose of the prescription are twice more likely to comply than those who do not understand.[8] This paper reviews the concepts, types, functions, approaches, & barriers of communication and suggest some tips for developing skills for effective communication.

Definition- Communication is regarded as two way process of exchanging or shaping ideas, feelings and information and arriving at a common understanding of the message. Communication is more than mere exchange of information. It is a process necessary to pave way for desired changes in human behaviour and involve individual and community participation to achieve predetermined goals. [9] Communication and education are interwoven. The goal of all communication is to bring about a change in the desired direction of the person who receives the communication. This change may be at the cognitive level in terms of increase in knowledge; it may be affective in terms of changing existing patterns of behavior and attitudes; and it may be psychomotor in terms of acquiring new skills. These are referred to as learning objectives.

Communication process- Communication is the basis of human interaction that involves a complex process of following components: Sender [source]; receiver [audience]; message [content]; channel [medium]; feedback [effect]. If any of these components are missing, effective communication cannot take place.[10]

Type of communication [11]

- One-way communication [Didactic method]: The flow of communication is one-way from the speaker to the audience. The familiar example is the lecture method in classroom. The drawbacks of didactic methods are knowledge is imposed; learning is authoritative with little audience participation; no feedback and does not influence human behaviour;
- Two-way communication [Socratic method]: In a two-way communication, both the communicator and audience take part. The audience may raise questions and add their own information, ideas and opinions to the subject. The process of learning is active and more likely to influence behaviour.
- Verbal communication: It is a traditional way of communication by way of mouth and more persuasive

than written and printed matter.

- Nonverbal communication: Communication can occur even without words. It includes a whole range of body movements, postures, gestures, facial expressions e.g. smile, raised eyebrows, staring, gazing, etc. Silence is non-verbal communication.
- Formal and informal communication: Communication has been grouped into formal [follows lines of authority] and informal [grape vine] communication. Informal networks e.g. gossip circles exist in all organization. The informal channels may be more active, if the formal channels do not cater to the information needs.
- Visual communication: The visual form of communication comprises charts, graphs, pictograms, tables, maps, posters, information booklets, magazines etc.
- Telecommunication and Internet: Telecommunication is the process of communicating over distance using electromagnetic instruments designed for the purpose. Radio, TV, Internet are mass communication media.

Functions of health communication[12]- The term health communication is often used synonymously with health education which itself is the foundation of all health-care programme and system including all specialties. Health communication has to cater to the needs of individual and/or organization i.e. to provide scientific knowledge or sensitive information; education; motivation, persuasion, counseling, raising morals, health development, building human relation and organization.

Barriers of communication- Health communication may often fail due to 'barriers' between the sender and the receiver that may result in problems and concern of varied nature. Better understanding of these barriers will prepare us to deal with any situation in a more prepared way. These barriers of communication may be at various levels

- Physiological: difficulties in hearing, expression
- Psychological: emotional disturbances, neurosis, level of intelligence, language or comprehension difficulties
- Environmental: noise, invisibility, congestion
- Cultural: illiteracy, level of knowledge and understanding, customs, beliefs, religion, attitudes, economic and social class differences, language variati-ons, cultural difficulties, between foreigners and nationals, between urban and rural.

Approaches and methods in health communication-There are various approaches and methods in health communication and each has its own advantages and disadvantages in a given setting for achievement of pre-determined health and family welfare goals. The approaches and methods in health communication may be broadly grouped as:

- Individual approach: Personal contact e.g. in OPD/IPD, home visits, personal letters
- Group approach: Lectures, demonstrations, discussion methods- group discussion, panel discussion, symposium, workshop, conferences, seminars, role-plays.
- Mass approach: Television, radio newspaper, printed material, posters, health museums and exhibitions, folk methods, Internet.

Effective communication- After reviewing the concepts, functions and barriers of communication the need for effective and meaningful communication has to be realized with some introspection in our life. As reported in a newscolumn some of the causes of communication gap amongst medical practitioners could be [a] some doctors are inherently reserve and less communicative and more over these skills are not a part of medical teaching; [b] some doctors are very busy and have taken many attachments and as such unable to devote time and commitment to the patients; [c] some doctors may be having lack of knowledge of the subject as well as may not be updated on recent advances in medicine. [13] Communication is both a science and an art that can be cultivated and developed with little effort and patience. Some tips for effective communication are[14]

Dos

- Always think ahead of what you are going to say
- Use simple words and phrases that are easily understood.
- Increase your knowledge on all aspect of subject you are dealing
- Make effort to appear enthusiastic while speaking ensuring clarity and audibility
- Check twice with the listener whether you have been understood accurately or not.
- In case of an interruption, always do a little recap of what has already been said
- Always pay attention to the content ignoring speakers appearance or manner in which message is delivered
- While listening, maintain your concentration on the subject and document important points.
- Always ask for clarification, if you have failed to grasp the point of view of the speaker
- Repeat what the speaker has said to check whatever has been said and what has been understood is the same or not.

Don'ts

- Do not interrupt the speaker, react instantly or mutter something in anger/anguish
- Do not use technical jargons while interacting with patients
- Do not speak too fast or too slow
- Do not speak in inaudible surroundings. You will not be heard.
- Do not have a mental state of ego or superiority complex while addressing a peer or patient
- Do not harbor pre-conceived ideas, biases or prejudice over an issue
- Do not assume that every body understands you
- While listening do not glance here and there. It may distract the speaker.
- Do not overload the patient with information
- Do not jump to a hasty conclusion that you have understood every thing

Conclusion-Effective communication is more than simply transmitting information to people in professional or social setting. No matter how clear the idea is in the mind of sender/ communicator, it may still be marked by poorly chosen words, omissions, lack of coherence, poor organization of ideas, awkward sentence structure, and failure to clarify the implication of the message. Each resident while undergoing training in respective specialty must make a conscious effort to learn the intricate art and science of effective communication. This will be helpful to candidate not only during the examination but also through out life, as s/he would have an edge in influencing people for behaviour change and making an impact on the society. We have heard the story of Eklavya, who learnt archery all by himself. He had no guru [Facilitator!], but only the intense wish to learn. This alone can drive the learning process but it will help only those few learners who are focused and driven by certain ideals. Similarly there may have been gurus who have made great disciple out of ordinary people. However, it may be difficult to get such disciples and gurus in present era.[15] Till such time we are able to find a right guru, the onus of learning effective communication, enrichment, development and growth lies on the learner in a system of teaching & training that is based on principle of adult learning.

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Recent advances in intravenous anesthesia

Efforts to develop new hypnotic compounds continue, although several have recently failed in development. Propofol has been reformulated in various presentations with and without preservatives. Pharmacokinetic and pharmacodynamic differences exist between some of these preparations, and it is currently unclear whether any have substantial advantages over the original presentation. The use of target-controlled infusion (TCI) has been extended to include paediatric anaesthesia and sedation. Application of TCI to remifentanil is now licensed. Linking of electroencephalogram (EEG) monitoring to TCI for closed-loop anaesthesia remains a research tool, although commercial development may follow. The availability of stereoisomer ketamine and improved understanding of its pharmacology have increased non-anaesthetic use of ketamine as an adjunct analgesic. It may be useful in subhypnotic doses for postsurgical patients with pain refractory to morphine administration.

5

Review Article

Basics of MR Spectroscopy

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MR Spectroscopy is a non invasive technique in which MR is used to determine the molecular structure of a compound or to detect the presence of a compound. It detects electromagnetic signals produced by atomic nuclei with an odd number of protons and neutrons and thus can obtain in situ concentrations of chemicals in normal and diseased tissue aiding medical diagnosis.MRS is similar to the spectroscopy used in chemistry/physics to study composition of matter in the past half a century. It has been in use longer than magnetic resonance imaging (MRI) and has a great potential for impacting patient diagnosis and treatment. In MRI images of tissues are generated using resonance of protons from water molecules, while in MRS water signals are suppressed and information is gathered from magnetic resonance signals of chemical compounds other than water. This gives the spectral signature of diseased tissues by evaluating the in vivo biochemistry. The information is provided as a biochemical spectrum rather than an imageTo obtain MRS information one needs to trade off spatial information (resolution) for chemical information. MRS procedures are evolving towards producing detailed chemical spectra for each image voxel [1] Currently, the resolution of these voxels is limited by the desired signal to noise ratio (SNR), the tissue concentration of the metabolites of interestThe concentration of water in tissues is of the order of 100M, which is 10,000 times the millimolar concentrations of most metabolites being studied by MRS. Thus images made from non water metabolites are severely limited by signal strength. Magnetic field strength is a major determinant of MR signal strength. As the field strength increases the MR signal increases[2]. Hence to get a good signal from compounds at micromolar concentration, it is desirable to image them at higher field strength preferably at 1.5T or higher. In addition to SNR improvements with increasing fields, the spectrum is spread out so that overlapping signals from adjacent peaks do not obscure fine details

Basic principles-Results in both spectroscopy and MR Imaging follow directly from the fundamental relationship that signal strength is directly determined by magnetic field strength Nuclei with odd no of protons and neutrons behave as spinning bar magnets and have a magnetic moment and interact with the external magnetic field. MRS requires that the body should be placed in a strong static externally applied magnetic field. The field should be homogenous and should not vary with time. Another oscillating magnetic field called the radio frequency (rf) field produced by the rf coil needs to be placed around the body part being examined. The rf coil produces the oscillating magnetic field which interacts with the different types of atomic nuclei . There is an exchange of energy with nuclei oscillating at the same frequency as the rf pulse. The rf pulse is switched off.Interaction between the magnetic field of atomic nuclei and the main external magnetic field produces an electromagnetic signal. This signal is detected by the RF coil to give the MR Spectrum. Gradient coils in conjunction with the RF pulse help in spatial localizationThe MR spectrum is a plot (intensity versus the frequency) of the number of nuclei in different magnetic field environments. By convention the signal field increases to the left.

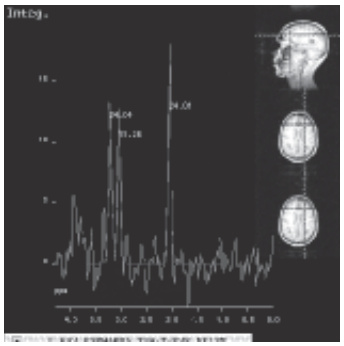

Fig-1, Normal MR Spectrum of the Brain showing the intensity of the resonance ie the signal on the Y axis and the frequency on the X axis. The amplitude of each peak reflects the number of nuclei at that particular chemical shift.

Nearly all hydrogen atoms give an MRS signal. Water and fat are present in abundance in the human body. Since the proton signal from water and fat are so large relative to the other metabolites technique need to be employed to suppress these signals to enable signals from chemicals in micro molar concentration to be picked up.

Chemical Shifts

According to the larmour equation $w_0 = ¡ B_0$,(Equation-1)

where B_0 is the strength of the externally applied magnetic field and ¡ the gyromagnetic ration that is characteristic for each type of atomic nucleus and w_0 is the precessional frequency. Consider bare protons in a magnetic field. If they all gave the same signal frequency then very little information would be available. It was soon recognized that protons which were part of a molecule had a different resonance frequency from the bare protons. So the effective frequency of protons in molecules was proportional to the effective magnetic field experienced by them, B_{eff}

$B_{eff} = B_0 + B_{local}$, (Equation-2)

The B_{local} can be either positive or negative. It is the result of two factors - the magnetic fields of electrons circulating around the nuclei and contributions from the magnetic fields of neighboring nuclei. Hence the measured signal w_{meas} can be expressed as

$w_{meas} = ¡ B_{eff}$, (Equation-3)

$w_{meas} = ¡ (B_0 + B_{local})$

$w_{meas} = ¡ B_0 + ¡ B_{local}$

$w_{meas} = ¡ B_0 (1+ s)$, (Equation-4)

Equation-4 thus reflects that the local magnetic field B_{local}, produced is generally directly proportional to the strength of the applied magnetic field B_0. The proportionality constant, s , is called the chemical shift for the nucleus and is typically expressed in parts per million (ppm) of the frequency in the applied magnetic field. Thus, s is independent of the applied field strength and is fixed for the molecular environment (structure) of the nucleus.When an external magnetic field is applied, most of the protons of the body align parallel to the main magnetic field and thus reinforce the applied magnetic field; called paramagnetic while a few align opposite the main magnetic field; diamagnetic. When the induced magnetic field opposes the external magnetic field, the effective field at the nucleus is lessened and the nucleus is said to be shielded. Conversely when the induced magnetic field increases the field at the nucleus, it is said to be deshielded.A particular atomic species is determined by the number of electrons that exist around it. However the actual electron density around the nuclei depends on the molecular environment (hydrogen, covalent, electron bonds) and the number of electro negative groups nearby. Protons of the body arise from two main sources: water (H_2O) and fat (primarily -CH_2- groups). The electronegative oxygen atoms of water tend to pull electrons away from the protons, so the applied magnetic field experienced by them is not shielded as much as the protons in the fat. Thus the proton signals of water and the methyle protons of fat will be at frequencies that are separated by 3.5ppm, regardless of the strength of the applied external magnetic field[1].

A basic step in spectroscopy is localization of the region of interest in all three spatial dimensions, yielding the volume of interest. This can be performed using two methods: single voxel spectroscopy (SVS) or chemical shift imaging (CSI). In clinical practice SVS is the easier and faster technique for obtaining metabolic information[3]. A homogenous magnetic field is an important prerequisite for obtaining clinically resolvable spectra. Shimming the field in the region of interest is often required to ensure homogeneity. Since the water concentration in living tissues (100M) is so much greater than the tissue concentrations of most metabolites of interest (10mM), the water signal is bound to completely dominate the recorded signals unless it is suppressed. The most common approach to suppress the water signal is to use chemical shift selective (CHESS) rf pulses[1]. Triglycerides in adipose tissues also produce a large signal. So signal from fat too needs to be suppressed . Application of chemical shift selective pulses centred on lipid peak result in their suppression. Fortunately this is not a problem in neuroimaging, as Brain has no fat.

SVS MR image is first obtained. The region of interest (ROI) is localized; defined as a rectilinear voxel. A rectilinear voxel is defined by placing three selective pulse along the three orthogonal axes. MRS signal is acquired only from this voxel. Signal from nuclei outside this voxel is supressed using gradient pulses called crushers. Many additional gradient pulses are incorporated into the pulse sequences to suppress unwanted echoes arising from outside the selected volume.SVS is easier and faster technique for obtaining metabolic information. The voxel (volume element) [4] being sampled has a minimum size of 1 cm^3 SVS have the advantage of excellent localization, field homogeneity, and water supression from a small well defined volume. One can obtain a spectrum within 3 to 10 minutes depending upon the chosen TR. It allows reliable quantification of metabolites. It is used best when global and not focal effects are of interest. (eg hepatic encephalopathy or brain injury from near drowning).

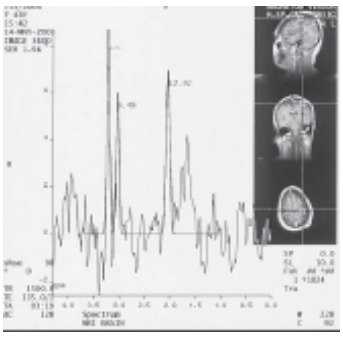

Fig-2, Single voxel spectroscopy showing a low grade glioma

MRSI / CSI / Multivoxel Spectroscopy-MRS signals are simultaneously acquired from a grid containing a large number of rectilinear voxels that include the tissues of interest. CSI has the advantage of obtaining multiple spectra in one data acquisition. One can obtain information from different voxels without running a spectroscopic scan. Single voxel spectroscopy gives one spectrum while CSI gives as many as 16 or more spectra depending upon the voxel size and the number of phase encoding steps used. A single voxel study can be repeated more easily if patient motion is suspected. Pt motion will compromise the data in CSI completely. There is poorer definition of the voxel in CSI than SVS. CSI provides a means of observing differences in metabolite levels throughout an organ or lesion when done properly. CSI can also be useful when multiple areas of interest such as radiation necrosis and recurrent tumor need to be differentiated. CSI can also help select the appropriate site for biopsy in cases of brain tumors by guiding the needle to the voxel where active tumor tissue is present and avoiding voxels showing necrotic tissue. CSI also helps gain insight into the heterogeneity of tumor tissue by showing high Cho/Cr ratios in voxels overlying high grade tumor tissues and low Cho/Cr ratios in voxels overlying lower grades of malignancy.

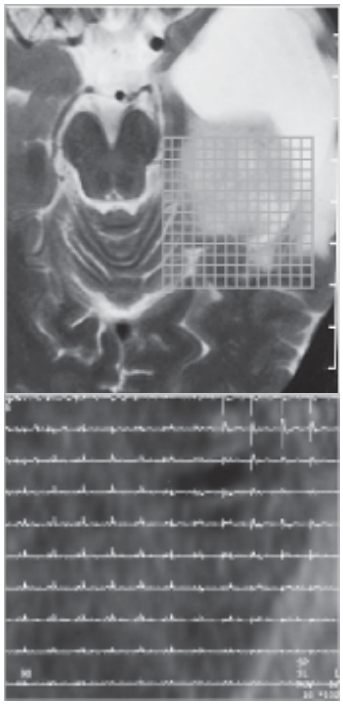

Fig-3, CSI: A grid placed over the region of interest with spectra obtained from each voxel in the grid , in a single data acquisition.

Advantages of CSI -to assess different regions of a mass,to study the brain parenchyma around the mass, to assess response to therapy,to look for tumor recurrence.

The acquisition of MRS spectrum takes very long.Because of low biological concentrations and less sensitive nuclei, signal averaging is needed to increase the signal to noise ratio. At least 128 signal averages are required to obtain interpretable spectra within a clinically acceptable time[5]. Repeated signal acquisitions thus increases time of acquisitions. To obtain spectral resolution, that is to separate the individual peaks in a spectrum a homogenous magn-etic field

through the ROI. Despite the huge number of biomolecules in tissues, few are identifiable in vivo because only freely mobile compounds that are present in substantial concent-rations give enough signals to be detected[6]. Spectroscopically visible metabolites include- ^{1}H, ^{31}P, ^{13}C, ^{7}Li and ^{19}F

^{1}H MRS is preferred because it gives the strongest and most easily detectable signal. It is performed using the same hardware as conventional MR imaging. Majority of neuroradiologic studies utilise ^{1}H MRS. Information of the identity of metabolites is obtained from their peak positions. Quantification of the metabolites from the area under the peaks.

Alanine, Glutamate, Glucose, Glu+Gln, Myo-inositol.The MR signal detected from a volume is directly proportional to the concentration of nuclei

STEAM- (Stimulated echo acquisition mode) pulse sequence uses a 90^{0} refocusing pulse to collect signals like a gradient echo. It allows visualization of metabolites with short relaxation times. Water suppression is more effective with this technique. Its disadvantages are a possible loss of signal intensity and high susceptibility to motion, quantum effects and diffusion

PRESS (Point resolved spectroscopy) sequence refocuses the spins with a 180^{0} rf pulse like a spin echo. It uses longer echo times and therefore allows visualization of metabolites with longer relaxation times. They are less susceptible to motion, quantum effects and diffusion and have a better SNR than stimulated echo mode.Most MR spectra are obtained with echo times of 135 and 270 milliseconds. Using long echo times the signal from most brain metabolites is lost. Conversely short echo times allow for identification of many other metabolites.

Observable Proton Metabolites

ppm	Metabolites	Properties
0.9 – 1.4	Lipids	Products of Brain destruction
1.3	Lactate	Product of anerobic glycolysis
2.0	NAA	Neuronal marker
2.2 – 2.4	Glutamine/GABA	Neurotransmitters
3.0	Creatine	Energy Metabolism
3.2	Choline	Cell Membrane marker
3.5	Myoinositol	Glial cell marker
1.2	Ethanol	Triplet
1.48	Alanine	Present in meningiomas
3.4 & 3.8	Glucose	Increased in Diabetics

Typically human MRS protocols use a magnetic field of 1.5 Tesla or higher.

The metabolites commonly studied in a standard Brain analysis include Choline, Creatine, NAA, Lactate, Lipid,

Metabolite significance-Each peak of the MR spectrum is characterized by its resonance frequency, height, width and area. Height or area under the peak is calculated to give the measure of the concentration of the metabolite

Creatine (resonates at 3.03 ppm)-Creatine-phosphocreatine is an energy-producing compound in cellular metabolism- provides a measure of the energy stores. Creatine is increased in hypometabolic states and decreased in hypermetabolic states. In normal spectra creatine is located immediately to the right of choline.

Choline(resonates at 3.2 ppm)-is a constituent of cell membrane serves as a marker of cellularity- elevated in tumors and inflammatory processes. Paradoxically Choline levels are low in very high grade tumors because of presence of necrosis. Therefore 1H MRS is not an independent diagnostic tool but rather a complementary modality to clinical MR imaging and PET. Clinical response to a tumor is seen by reduction in the level of choline before significant changes are evident on MRI

NAA (resonates at 2ppm)- is the most prominent resonance in proton MRS of the brain. It is a neuronal marker and decreases with any disease affecting

neuronal integrity such as neoplasms, infarcts, epilepsy and dementia.There is a marked increase in NAA only in canavan's disease.NAA is generally accepted to be localized to the neurons and any destructive or infilterative lesion might therefore be expected to result in graduated reduction in NAA signal intensity. For this reason NAA is less useful in evaluation of brain tumors

Lactate(resonates at 1.32 ppm)- It is a doublet of of two distinct resonance peaks at 1.32ppm. Another peak for lactate occurs at 4.1 ppm. Because this is very close to water it is generally suppressed. Altering echo time generally confirms a peak at 1.32 ppm as lactate. At an echo time of 270 milliseconds, lactate projects above the base line, but at an echo time of 135 milliseconds it is inverted below the base line. This phenomenon is called j coupling. It is a product of anaerobic metabolism-seen in hypoxia. Lactae can be seen even after treatment due to treatment induced ischemia in tumor tissue. MR spectroscopy shows elevated lactate in patients who have received 40 Gy or more to the brain. The lactate peak can be identified before MRI shows any changes.Lactate and lipids increase in anaerobic metabolism and are present in some tumors such as high grade astrocytomas and meningiomas.

J Coupling-Splitting of the signal peak arises from the phenomenon of spin-spin coupling between neighbouring nuclei. In addition to the small electron magnetic field influencing the net magnetism at the nucleus, the small nuclear magnetic fields from nearby protons can also contribute to the net field strength. The precise field strength contributing to a nuclei depends upon the neighbouring nuclei and the chemical bonds between them. A resonance peak is often split into a number of equally spaced peaks referred to collectively as multiplets. The extent of coupling depends upon the proximity of the spins in space with the most interaction occurring if the two spins are chemically bonded. When a proton interacts with a nearby proton, they are influenced by each other's field. The net effecvt of this interaction depends upon whether the respective fields are oriented with or against the applied magnetic field direction. Consider a proton A being at one location in a molecule. If there is one neighboring proton, the neighboring magnetic field can either add (+) or subtract (-) with the proton A's field & each case is equally likely. Herefore one neighboring proton will split proton A's signal into two equal and separate peaks. The coupling constant J represents the distance in Hertz between the adjacent peaks and is characteristic of the type of the chemical bond. Because of the J coupling the CH_3 signal of lactate appears as a doublet separated by 7 Hz. Lactate assignment to the position 1.32 ppm is exploited by phase modulation where at TE 135 ms it is inverted and at 270 ms it becomes upright.

Myoinositol peak occurs at 3.56 ppm. It's levels are raised in Alzheimer's Disease and Hepatic Encephalopathy. Decreased myoinositol levels are seen with protective action of lithium in mania and the development of diabetic neuropathy. It is also reduced in hyponatremia. The myoinositol peaks are also significant in head and neck cancers

Lipids have very short relaxation times and are normally not observed until short echo times are used. The protons of lipids produce peaks at 0.8, 1.2, 1.5 and 6.0 ppm. These metabolites may be increased in high grade astrocytomas and lymphomas and may reflect necrotic processes. Lactate and mobile lipids are normally not present in the brain. They are shown to increase in some tumors such as high grade astrocytomas and meningiomas [5]

Glutamate and glutamine peaks are located between 2.1 and 2.5 ppm

Metabolite Ratios

	Normal	Abnormal
NAA/Cr 2.0		< 1.6
NAA/Cho	1.6	< 1.2
Cho/Cr	1.2	> 1.5

Clinical applications of MRS & MRSI

- Brain Tumours-D/D between infarction/tumour / infection; Degree/grading of malignancy; Differentiation between radiation necrosis Vs recurrence of tumour; Insight into the metabolic heterogeneity of tumours; Monitoring response to therapy

- Lateralisation of epileptic focus in cases of intractable seizures
- Degenerative disorders in children and elderly individuals.
- Psychiatric Disorders

MRS in Brain Tumors-As malignancy increases, NAA & Creatine decrease and Choline lactate, and lipids increase.Very malignant tumors have high metabolic rates. This results in depletion of energy stores. As a result Creatine decreases. Hypercellular tumors with rapid growth result in increase in choline .Lipids are found in necrotic portions of tumors. Lactate appears when tumors outgrow their blood supply. Elevated choline in the presence of lactae correlates with a higher degree of malignancy. Raised lactate is commonly observed in GBM. Elevation of lactate may reflect tumor hypoxia. NAA levels are low in all tumors but the lowest in high grade astrocytomas. Presence of lactate generally reflects necrosis and therefore a high degree of malignancy

Meningiomas-Choline is also increased in some slow growing tumors such as meningiomas. The signal of choline is markedly increased (upto 300 times) in recurrent meningiomas. Lactate and alanine may also be elevated especially in the fibrous types of meningiomas.

Lymphomas-Spectroscopic appearance of lymphomas is similar to that of primary high grade astrocytomas and metastases. MR spectroscopy shows a marked elevation of choline and lipids and a significant reduction in creatine and NAA. MR spectroscopy is successful in assessing the response of lymphoma to treatment. Successfully treated lymphomas show progressive decrease in choline and lipids.

Multivoxel spectroscopy-detects infiltration of maliganant cells beyond enhancing tumor margins;Elevated choline-marker of recurrent tumor; Radiation Change - low NAA, Choline, Creatine; Radiation Necrosis-elevated lactate and lipid as well; Metastasis elevated Cho/Cr from the metastatic focus but normal spectra from the brain tissue adjacent to the enhancing edge of the metastatic focus. Gliomas show elevated Cho beyond tumor margins unlike mets. Non glial tumors show little or no NAA

Grading Brain Tumors-MRI has a limited accuracy in defining tumor boundaries or differentiating mild and moderate tumor infiltration from normal brain tissue. It is also known that gadolinium enhancement does not always correlate with the highest cellularity and infiltrative tumors may extend far beyond the contrast enhancing areas. MRS correlation with histology has shown that increasing Cho content correlates directly with increasing tumor grade.

Radiation Necrosis-histologically radiation injury is characterized by damage to the vascular endothelium that may result in ischemia and necrosis**.** MR spectroscopy shows elevated lactate in patients who have received 40 Gy or more to the brain. The lactate peak can be identified before any morphological changes are picked up by MRI. MRS helps in differentiating radiation necrosis from recurrent/residual tumor by demonstrating severely depressed levels of NAA, Cho and Cr in radiation necrosis. In addition radiation necrosis shows a broad peak between 0 to 2 ppm corresponding to cellular breakdown products probably consisting of free fatty acids lactate and amino acids

MTS MRS can be used to localize seizure focus in temporal lobe epilepsy as an alternative to PET and SPECT. NAA is reduced in seizure foci. This represents a neuronal loss or damage. The epileptogenic hippocampus shows a decrease NAA/Cho ratios and an increased or normal Cho/Cr . there may be raised levels of lactate after an episode of acute temporal lobe epilepsy.

Abscesses Metabolites which can be seen only by using short echo times. Metabolites include acetate, lactate, pyruvate and succinate. Amino acid signals at 0.9ppm-leucine, isoleucine, valine. There is reversal of lactate peak in the abscesses after treatment.

AIDS- Patients demonstrate marked metabolic alterations

even with mild AIDS related dementia Virus infected macrophages cause neuronal damage resulting in drop in NAA levels. There is decrease in NAA/Cho and NAA/Cr and increase in Cho/Cr in subcortical grey matter. After therapy there is improvement of NAA/Cr ratios. HIV positive newborns have normal brain MRI but abnormal spectra as early as ten days after birth!

Chronic Infarcts- Reduction of Cho, Cr, NAA compared to the contralateral side. NAA is reduced to a greater extent than Cho or Cr. Subacute to chronic infarcts demonstrate persistent levels of lactate within the infarct. Brain infarcts are associated with a marked decrease in cellular density in the region of the infarct which accounts for the reduced metabolite concentration. The finding that Cho/NAA and Cr/NAA is increased in regions of infarct is due to the fact that there is greater reduction of NAA compared to the contralateral side than Cho or Cr. This is due to greater loss of neurons than glial cells in infarcts[7]

Limitations of MRS

- Studies[8] have found that glioblastoma multiforme showed paradoxically lowest average normalised choline values. This is most likely due to presence of extensive necrosis seen in this tumor and partial volume limitations. Similar limitation is seen in PET as well- most metabolic tumors outgrow their blood supply to produce necrotic centers resulting in reduced metabolic activity. Thus potential to miss highly malignant lesions with PET/MRS suggests caution in using either technique alone.
- MRS cannot be performed in or adjacent to bone, air , large vessels and hemorrhagic lesions.
- Susceptibility artifacts from metal and shunts may obscure the spectra.
- MRS has low sensitivity for detecting molecules in tissues

Rule of thumb for 1H MRS signal detection- at least 1 micromole of the molecule of interest should be present in the volume of interest. Therefore only few of the most heavily concentrated molecules are readily detected with MRS. It cannot replace brain biopsy for histological diagnosis, but may be able to better delineate and define tumor boundaries and separate an infiltrative growing glioma from normal brain tissue thereby helping in presurgical planning of brain neoplasms

Comparison between MR Imaging and MR Spectroscopy

MRI	MRS
Deteciton of water signal 1H	Detection of signal from biocehemicals-1H, 31P, 13C, 7Li and 19F
High spatial resolution	Low spatial resolution
mGradients are required for localisation of signal in MRI and MRS MRI uses them during the acquisition period	MRS also needs gradients for signal localisation but they have to be switched off during the acquisition period to ensure homogenity of the external magnetic field during signal acquisition
Temporal resolution is in seconds	Temporal resolution is in minutes due to repeated signals and signal averaging to improve SNR
In MRI pictures are available immediately	MR Spectroscopy requires post processing of the FID data to maximise the information content

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Surgery in ancient India

Varanasi on the banks of the Ganges is one of the holiest places in India. It is both the city of Buddha and a destination of pilgrimage for millions of Hindus who come to bathe in the holy river. It is also the home of Ayurveda, one of the oldest medical disciplines. Ayurveda means 'science of life', and its approach to the body is philosophical and holistic. Among the greatest of its ancient writings is the *Sushruta Samhita,* which describes the tradition of surgery in Indian medicine. Its author is believed to have been the scholar Sushruta, who lived over 3,000 years ago. Sushruta is said to have been given his knowledge by an incarnation of the god Vishnu. However, it is also suspected that he was simply reporting medical wisdom that had been passed down by word of mouth for centuries. In the book's 184 chapters, 1,120 conditions are listed, including injuries and illnesses relating to ageing and mental illness. For instance, there are accounts of 76 eye conditions, 51 of which were treated surgically. The book also describes 101 blunt and 20 sharp surgical instruments, many of which are surprisingly similar to instruments used today. Other treatments are also discussed, comprising 700 healing plants, 57 preparations derived from animal sources and 64 preparations from minerals. One of the plants was used to produce suturing thread that had immunity-boosting properties. Others provided pain relief and still others were natural antiseptics.Sushruta also recommended using leeches to keep wounds free of blood clots. This has only recently been rediscovered and is now used, especially in plastic surgery, to help reduce congestion in tissues, especially in wounds and in flaps used for reconstructing body parts.

Sushruta's general advice to physicians would certainly apply to doctors anywhere and in any age-A physician who has set out on this path should have witnessed operations. He must be licensed by the king. He should be clean and keep his nails and hair short. He should be cheerful, well-spoken and honest.

The compendium goes on to describe some extraordinary surgical techniques, including a revolutionary nose reconstruction, or rhinoplasty. It was common practice in ancient India to punish criminals by amputating the nose. As a result, Ayurvedic surgeons had plenty of opportunities to practise this.

6

Review Article

Image Guidance in Radiotherapy- From Planar to Multidimensional Radiotherapy

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Radiological imaging and radiation therapy share a common past. The discovery of X-rays by W C Roentgen in 1895 and the historical radiograph of his own hand was the beginning of radiation for diagnosis and therapeutic purposes (Balter S, 1989). Since then, over more than 100 years, there have been revolutionary changes in diagnostic imaging and therapy delivery technology. At the same time, there has been significant improvement in the understanding of the cancer biology and its management strategies. The changes brought about in radiotherapy by i) the transition from the usage of largely anatomical images to the new types of images that can provide biological data about the tumour, and ii) from rectangular fields with uniform intensity for radiation delivery to intensity modulated geometrically shaped beams will be discussed in this article. Generally, the term Image guided radiotherapy (IGRT) is used in a very specific context in radiotherapy. It usually means using on-board imaging system (planar or 3D) to correct for inter-fraction (set-up /organ motion) errors while delivering the radiation dose. However, in this article it will also include the imaging used for delineation of the tumour/target and normal structures.The aim in radiotherapy is to deliver certain tumouricidal dose to a target volume and at the same time spare the surrounding normal tissues as much as possible to minimize treatment related toxicities. On many occasions, the normal tissue tolerances are usually the limiting factors for the inability to deliver the desired dose to the tumour. All the technological innovations in radiotherapy primarily attempt to escalate the target dose without increasing the toxicities. Image guidance in radiotherapy is a crucial means to achieve this wherein through the available images, the radiation dose is delivered to the delineated target. This process of using X-ray images for radiotherapy delivery guidance can be said to be as old as radiotherapy; starting with simple planar images that could barley differentiate between bone and soft tissue to today's CT, MRI and PET imaging. It was CT and MRI in the last over three decades that provided a revolutionary improvement in our ability to visualize human anatomy. Advances in Nuclear Medicine imaging that include single photon emission tomography (SPECT) and positron emission tomography (PET) hold enormous opportunity for improving the management of cancer in general and the radiotherapy practice in particular. For a long time, external beam radiotherapy was delivered with rectangular shaped uniform intensity beams: starting with superficial (upto 120 kVp) and orthovoltage X-rays (150-500 kVp) followed by telecobalt machines and linear accelerators in the 1950s (Bentel GC, 1992). Beam shaping to conform the dose to the tumour shape, was usually carried out by using shielding blocks. This was coarse, time consuming and always not satisfactory. Similarly, in brachytherapy, from the preloaded radium applicators, it was extremely difficult and in most cases impossible to shape the dose envelope to that of tumour volume. However, the technological advances during the last few decades have significantly removed these handicaps of conformality and improved the therapeutic efficacy. These include the linear accelerators (linacs), treatment simulators, high dose rate afterloaders, computerized treatment planning etc. The incorporation of multileaf collimators (MLC) in the linac head heralded the birth of present day 3D conformal radiotherapy (3DCRT) in the early 1990s (Mohan R et al 1998).

Most recently, it is the intensity modulated radiotherapy (IMRT) that has gained popularity for achieving still better conformality (Nutting C et al., 2000). Also, particle radiotherapy using protons, carbon and some other heavy ions, though exorbitantly costly at the moment, may gain wider acceptability for its better physical and biological dosimetry properties.

Target volumes in radiotherapy - The International Commission of Radiological Units and Measurements (ICRU) in its report number 50 (1993) recommended a method for dose prescription and reporting in radiotherapy. In this report they describe the gross tumour volume (GTV) as the "gross palpable or visible/demonstrable extent and location of malignant growth". This volume is incorporated in the volume considered at risk, the clinical target volume (CTV), defined as "a tissue volume that contains a demonstrable GTV and/or subclinical microscopic malignant disease, which as to be eliminated". This volume thus has to be treated adequately in order to achieve the aim of therapy, cure or palliation. The GTV and the CTV are anatomical and biological concepts. In addition the ICRU defines the planning target volume (PTV) as "a geometrical concept, and it is defined to select appropriate beam sizes and beam arrangements, taking into consideration all the possible geometrical variations, in order to ensure that the prescribed dose is actually absorbed in the CTV". The PTV includes the CTV plus margins for patient motion, organ motion, organ shape and size variation and uncertainties in beam placement. A new term i.e. biological target volume BTV has also been coined in recent literature. This may help in escalating the dose in a specific volume of a target depending upon it biological property such as higher tumour burden.Aiming to deliver a known homogeneous dose to the PTV has so far been the paradigm in radiotherapy. But the emerging biological imaging may reveal the non-uniformity in terms of tumour burden, radiosensitivity within the PTV and hence the need to deliver non-uniform dose through IMRT may bring about a paradigm shift in the dose delivery concept. In fact, current technology for delivering conformally shaped external beam radiotherapy (IMRT) may have exceeded our ability to localize tumours and normal tissues by conventional imaging techniques. The ability of IMRT to "paint" or "sculpt" the dose leads to the question as to what needs to be painted or sculpted. It is believed that non-invasive biological imaging may provide the pertinent information to guide the painting or sculpting for the optimal dose distribution. Important for IMRT, the spatial distribution of radiobiological phenotypes will be the basis for designing the dose distribution conforming both the physical and biological attributes of the tumour. The following few paragraphs describe how the various imaging modalities and on-board imaging systems have impacted the practice of radiotherapy.

Target Delineation

CT, MRI and Ultrasound(US) imaging techniques-CT has played a pivotal role in the process of defining the extent of the tumour target volume. It has many advantages such as high spatial integrity, high spatial resolution, excellent bony structure depiction and the ability to provide electron density information used for radiation dose calculations. With latest 64 or even 128 slice CT machines in the market, time-resolved or 4D CT has become a reality to take care of the organ motion during cardiac or respiratory cycles for intrafraction image guidance in radiotherapy.MRI provides superior soft tissue discrimination especially for CNS structures and within the abdomen and pelvis and has been widely used in the diagnosis and tumour delineation. With increasing use of 3T MR images and fast-cine MRI, still better quality images with temporal processes such as breathing can be imaged. The development of some specialized MRI scans such as diffusion and perfusion MRI, dynamic contrast MRI, MR angiography, MR spectroscopic imaging (MRSI) and function MRI (fMRI) has attracted much attention for biological and

functional imaging purposes. Ultrasound (US) is another useful imaging modality for radiation therapy particularly for prostate imaging. Transrectal US is the imaging modality of choice for prostate seed implant (brachytherapy). Incidentally, one of the early on-board imaging systems in EBRT for prostate was based on US imaging.

Biological Imaging-It is defined as the *in vivo* characterization and measur-ement of biological processes at the cellular and molecular level. It is an emerging multidis-ciplinary field resulting from the developments of molecular biology and diagnostic imaging that has the potential to revolutionize cancer detection, staging, treatment decision making and assessment of response. Biological images broadly include those in the metabolic, biochemical, physiological and functional categories. They should also encompass molecular genotypic and phenotypic images currently under investigations. For radiotherapy, images that can give information about factors such as hypoxia that influences radiosensitivity and treatment outcome can be called as radiobiological images (Ling CC et al., 2000).MRSI and PET are two valuable modalities for radiation planning. ^{1}H MRSI combines the advantages of obtaining biochemical data by water suppressed ^{1}H MR spectroscopy with the spatial localization of the data. A study on impact of MRSI on the target volume (CTV) delineation in high-grade glioma demonstrated that although T2 weighted MRI estimated the risk of microscopic disease as being as much as 50% greater than MRSI, metabolically active tumour tissue still extended outside T2 region in 88% of patients by as much as 28 mm. In addition T1 weighted MRI suggested a lesser volume and different location of active disease as compared to MRSI (Xing et al., 2006). MR spectroscopy is similarly useful in characterization of prostate tumours. However, despite the growing evidence that *in vivo* MRSI provides unique information on metabolism that will affect treatment planning, this modality has not gained wide spread usage.On the other hand, PET has gained popularity for being used in treatment planning process. Since PET contains no anatomic information about normal structures, it needs to be fused with corresponding CT images for treatment planning. Hybrid PET/CT systems are a result of this necessity. The most commonly used tracer for PET studies is fluorine-18 labeled deoxyglucose (FDG), which provides a means to study the metabolic activity of the tumour *in vivo.* In several studies on the impact of functional imaging with FDG-PET on target volume, it has been shown that over 50% radiation planning were changed with PET-CT fusion as compared to CT alone in the case of non small cell lung cancer (NSCLC). The changes included alteration in AJCC TNM staging and modification of CTV. It has also been shown that a sizeable proportion of patients with locally advanced NSCLC became ineligible for curative radiotherapy because of detection of either distant metastatic disease or extensive intrathoracic disease. Similar results have been reported for oesophagus cancer (Xing L et al, 2006). Of course there are some pitfalls of the FGD- PET in that the tracer can be nonspecifically taken up by several benign conditions such as inflammatory disease, pneumonia, brown fat, muscle. Also, slow growing indolent tumours may be missed by FDG-PET due to only mild increase in their glucose metabolism. The recent development of fluorothymidine (FLT) provides a new opportunity for improving sensitivity and specificity of PET imaging of cancer. Agents, such as antisense molecules, aptamers, antibodies, and antibody fragments can be aimed at molecular targets for biological imaging. Tumour receptors and certain cellular physiologic activities, including metabolism, hypoxia, proliferation, apoptosis, and angiogenesis provide such targets.

Biological Conformal Radiotherapy (BCRT)-As described above biological images may provide necessary information regarding the non-uniformity of tumour cells within a PTV and then IMRT capability may be used to escalate the dose

selectively within the PTV for achieving better control rate at the same or lesser toxicity levels. For example, MRI/MRSI images of choline/citrate ratio can be taken as surrogate for tumour burden or low pO_2 within the tumour can be delineated using PET or MRI or using iodine-124-iododeoxyuridine (^{124}IUdR) tracer in PET, tumour repopulation during a course of radiotherapy can be assessed. This information then can be used to define biological target volume (BTV) and deliver higher doses of radiation to the specific volume within the PTV. Figure 1 illustrates the concept of BTV schematically which can improve the dose targeting to certain regions of the PTV.

On-board Imaging-On-board imaging means acquiring and analyzing patient images in the treatment position. This is aimed at reducing inter-fraction uncertainties resulting from errors in patient set-up, organ motions, beam placement etc. The concept of on-board imaging is few decades old though its practice has assumed greater significance recently with the advent of 3DCRT and IMRT wherein higher doses of radiation with tighter margin around CTV is aimed to be delivered. Consequently, misdelivery due to set-up errors or organ motion may result in unacceptable outcomes in terms of tumour control or toxicities. Even in a seemingly obvious non-moving organ like prostate, several studies have shown organ position shift of more than 1.0 cm in day-to-day treatment (Ten H. et al., 1991).In the initial days, portal films in the treatment position were taken with the megavoltage X-ray (treatment) beam. The 2D image quality was just sufficient for bone and soft tissue contrast and helped in detecting any gross mismatch between the planned and treated area. Electronic portal imaging devices (EPID) with a fluorescent screen, a mirror and a CCD camera were the next system that were more convenient than the film, giving instant image and hence on-line correction for any shift became possible. However, the introduction of a-Si based flat panel detector system has revolutionized not only the field of radiology but also the on-line real-time portal imaging system. They are compact and offer far superior image quality even with megavoltage beam. The flat panel detectors have given birth to cone-beam CT (CBCT) technology which now offers excellent real-time 3D images on a linear accelerator and helps in finding the off-set between the planned target volume and the volume being treated. At present, there are many variations of the real-time (on-line) image guidance in radiotherapy. Some vendors add a special kV X-ray source for CBCT on the linac gantry, some other use the megavoltage treatment beam for imaging as well and still other prefer a diagnostic CT on-rail in the treatment room wherein the treatment table moves the patient first into the CT gantry and after image acquisition, into the treating position. In Tomotherapy, a compact linac is mounted into a CT gantry and the imaging and slice by slice treatment of the patient by a fan beam of megavoltage radiation is akin to a diagnostic helical CT.

Conclusion-The technology of on-board real-time image guidance has taken the accuracy and precision in the delivery of radiotherapy to unprecedented levels. In combination with IMRT technology and the upcoming biological imaging, the stage is set for practicing biologically conformal radiotherapy. At present, it can be however, said that our ability to deliver physically conformal dose has probably exceeded our ability to delineate tumour target biologically. Therefore, more efforts are needed in the area of imaging to reap the full benefit of IM-IGRT delivery technology and be in a position to deliver multidimensional conformal radiotherapy (MDCRT) that adds biological dimension to conformality with the existing 4D anatomical dose conformality.

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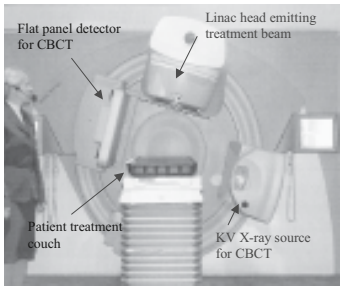

Fig-2: Linear accelerator with on-board imaging system

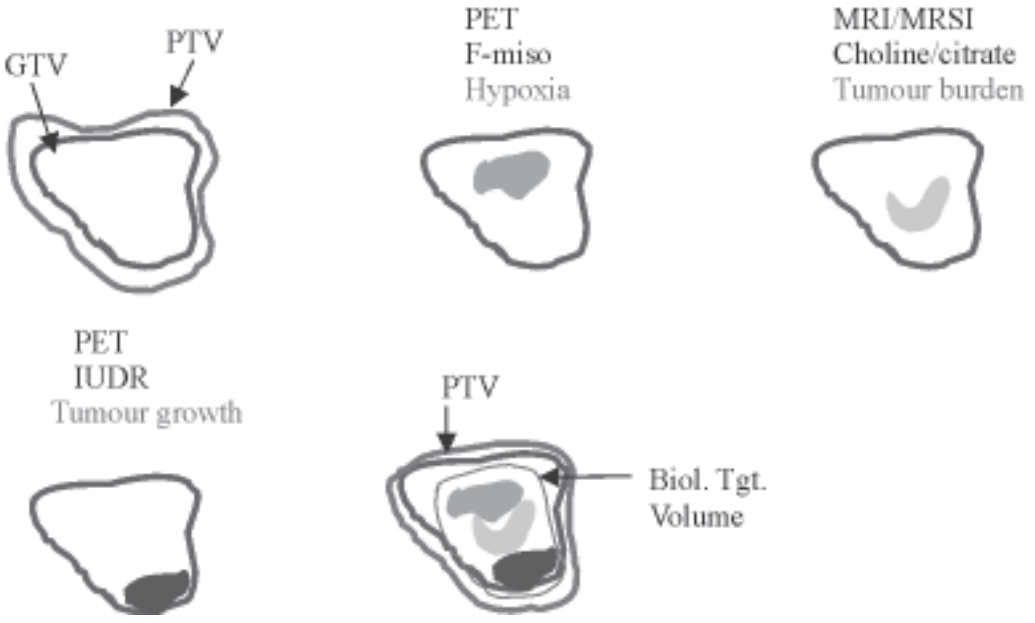

Fig-1: A schematic illustrating the concept of biological target volume (BTV). The regions of hypoxia may be derived from PET- ^{18}F-misonidazole study, higher tumour burden from MRI/MRSI data of choline/citrate ratio, and high proliferation from PET-^{124}IUDR study (Schematic concept Ling CC et al., 2000).

Imaging and Interventions in HCC

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Hepatocellular carcinoma is the commonest primary hepatic neoplasm and fifth commonest malignancy. Its incidence is highest in Far East and Asia, and increasing in the western world, because of increasing incidence of hepatitis B & C. HCC has a poor prognosis with median survival rate less than a year after diagnosis. Men are more commonly affected (M: F 2-8:1). The average age at presentation is 30-50 years in the asian population and 50-70 years in the west.

Pathophysiology- Vast majority of patients have underlying cirrhosis. Hepatitis B, Hepatitis C and alcoholic liver disease are the common etiologies, with Tyrosinemia, Hemochromatosis, excessive androgens, á1-antitrypsin deficiency and exposure to aflatoxins, thorotrast, oral contraceptives and vinyl chloride also being implicated. Development of HCC is a multi step process based on gradually increasing size and cellularity: from a regenerative nodule, low grade dysplastic nodule, high grade dysplastic nodule, to HCC. Along with this process, neoangiogenesis and capillarization leads to a sequential decrease in portal blood supply and an increase in arterial supply. As a result, HCC derives its blood supply almost exclusively from the hepatic artery – a factor used in imaging for lesion characterization. HCC is a 'capsulated' lesion which can have a very heterogeneous appearance due to presence of hemorrhage, necrosis, fat and calcification. It is commonly a solitary lesion but may also be multi focal or even diffuse.Lung, bone and adrenals are common sites of metastases, whereas nodes around porta, celiac axis and para aortic region are most common sites of nodal spread.

Imaging-Imaging plays a central role in Screening / Surveillance, Evaluation & Staging, Pre treatment Planning, Treatment and Post treatment Follow up of HCC. Various imaging modalities can be used, either alone or in conjunction.

Ultrasound-Ultrasound is widely available, inexpensive and does not utilize ionizing radiation. It therefore is a good screening modality. A combination of USG and Alpha-fetoprotein levels every six months is recommended as screening procedure in patients with cirrhosis. Ultrasound however, has its limitations: it is highly operator dependent, limited by tissue contrast, ribs and bowel gas and has poor sensitivity and specificity. Detection of a lesion on ultrasound therefore is often a starting point in evaluation for HCC.Appearance of HCC on sonography depends upon its contents. It is commonly hypoechoic, (Fig-1a) due to dense cellular elements, necrosis and sinusoidal dilatation. It may also be heterogeneously hyperechoic (fig-1b), when it contains fat, hemorrhage or fibrotic elements. It may have a surrounding capsule, which is commonly hypoechoic.

Color Doppler-imaging can play a role by demonstrating vascular invasion, hypervascularity and arteriovenous shunting. Ultrasound is also invaluable in providing guidance for percutaneous biopsy and for treatment delivery like ethanol injection and Radiofrequency ablation.

CT-Introduction of MDCT has made a quantum difference to imaging by its increased speed, coverage and resolution along with the ability to reconstruct images in multiple planes and using different algorithms like maximum and minimum intensity projections. This has enabled multiphase CT of liver, which, by better evaluation of the enhancement pattern results in improved characterization. However, this also demands meticulous technique, particularly in the timing of scans.Technique: Four phases of contrast enhancement in liver are recognized. The early arterial phase starts at 15 sec, lasts 7 – 12 sec and reveals enhancement of

hepatic arteries with no parenchymal enhancement (Fig-2a). Late Arterial phase starts at 30 seconds, lasts 12 sec. Arterial enhancement persists, along with early portal venous and parenchymal enhancement, but no hepatic venous enhancement. Portal Venous Phase starts at 60 – 70 sec and represents peak of parenchymal and portal-venous enhancement with opacification of hepatic veins. The fourth or delayed phase, also called the equilibrium phase starts at approximately 150 seconds. For evaluation of possible HCC, at least a three phase study is recommended, with scans obtained in late arterial phase, portal venous phase and the delayed phase in addition to the plain scan. Although the early arterial phase does not significantly add to the detection, it is still useful for evaluation of the arterial blood supply and vascularity.Usually, 120 – 150 cc of contrast material containing 370mg/ml of iodine is used, injected at a rate of 4-6 ml/sec, followed by a saline flush. To obtain optimal enhancement in various phases, fixed timing, bolus triggering or test bolus may be used.HCC is seen as iso to hypodense lesion on plain scans (Fig-2a). It shows intense enhancement on arterial phase, appearing hyperdense as compared to the liver parenchyma, which in this phase does not show enhancement. For smaller lesions, the enhancement is usually uniform, where as larger lesions show heterogeneous enhancement due to various elements within the tumour. (Fig-2b). A variegated pattern may also be seen, due to abnormal internal vessels. A rare, but specific finding is a 'nodule within a nodule' – an enhancing nodule within an iso/hypodense nodule, which represents an HCC within a dysplastic nodule. The capsule, when present is seen as a hypodense rim.On the portal venous phase, HCC becomes iso to hypodense (early wash out) against the background of enhancing liver parenchyma (Fig-2c). Venous invasion can be well assessed on this phase, as can the nodal spread. However, caution is recommended in commenting about the nodal spread, as patients with cirrhosis may have locally enlarged nodes without HCC. On the delayed phase, HCC appears hypodense in relation to the rest of the liver parenchyma, even as the 'capsule' reveals progressive enhancement. – a finding specific for HCC.

MRI- MRI has distinct advantages over CT in not employing radiation and a safer contrast agent with much lower risk of contrast nephropathy (Although recent reports of Gadolinium induced NSF/NFD should make one cautious). It is more sensitive and specific than CT, especially in differentiating between cirrhotic nodules (RN, DN) and HCC.Technique-T1 weighted Fast Spoiled Gradient Echo, Single Shot Fast Spin Echo and Double Echo T1 – In phase – Out phase sequence for assessment of Fat – water content are routinely used, followed by Post Gadolinium Dynamic Multiphase T1 weighted sequence. This, in principle is identical to multiphase CT, using the hypervascularity and arterial enhancement for lesion characterization.Appearance of HCC on T1 WI is variable, depending upon the contents (Fig-3a). Hyperintensity suggests presence of fat, copper or glycoproteins. It is invariably hyperintense on T2WI (Fig-3b). Capsule when present, appears hypointense. On dynamic post contrast images, like in CT, it shows intense enhancement in arterial phase, early wash out in the portal venous phase and has an enhancing capsule (Fig-4).

Pre treatment Evaluation- Surgery remains the best treatment option and both CT and MRI are used for pre surgical evaluation. In addition to the no., size and distribution of lesions, assessment of tumour vascularity, venous invasion and extrahepatic spread is made. Liver volumetry, vascular anatomy and presence of any other lesions or findings which may influence surgery may also be required.

Imaging Guided Interventions -DSA, Ultrasound, CT and more recently, MRI have been used for guidance in Interventional procedures.

Biopsy-If the imaging features are characteristic, biopsy is seldom required and should be avoided in potentially operable lesions, because of the risk of tumour seeding. CT and Ultrasound can both be used as guidance modalities. Ultrasound has the advantage of being widely available, non ionizing nature and real time guidance and should be

preferred when lesion is visualized on sonography.

Chemoembolisation-Drugs and other agents can be delivered using super selective micro catheters. It can double life expectancy and can be repeated aggressively (Fig-5).Percutaneous Ablation: Option for patients with early stage HCC who are not resection or transplant candidates. Destruction of the tumour tissue is achieved using either chemical substances (Ethanol, Acetic Acid) or by modifying temperature (Radiofrequency, Laser, cryotherapy) Ethanol injection is simple, low cost and effective, achieving tumour necrosis in 90 – 100% of lesions less than 2 cm., while RF ablation is preferred in lesions between 2- 5 cm. (Fig-6)

New Developments-Interesting developments are taking place in all imaging modalities, which may influence liver imaging in future. Newer contrast agents in ultrasound, Perfusion imaging in CT and development of parallel imaging, better sequences and imaging at 3T in MRI are likely to influence evaluation of liver lesions.

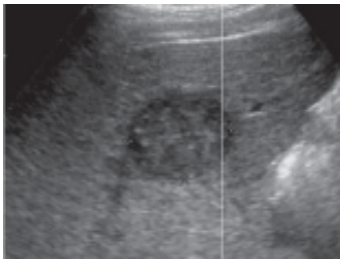

Fig-1a, Hypoechoic HCC

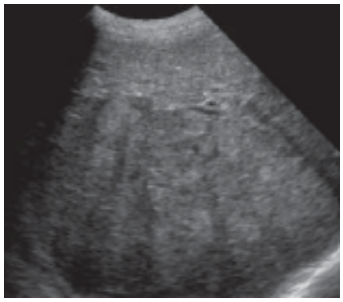

Fig-1b, Heterogeneously hyperechoic HCC

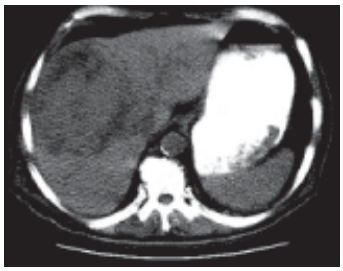

Fig-2a,Large HCC on plain CT

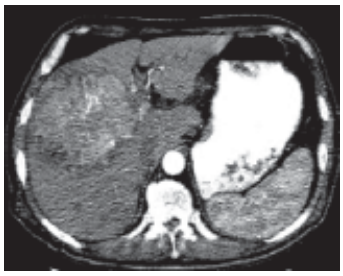

Fig-2b Enhancement on early arterial phase

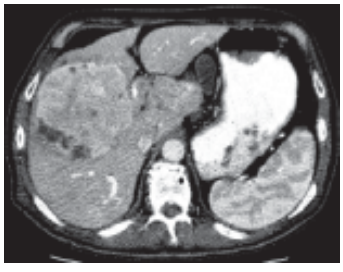

Fig-2c,Late arterial Phase

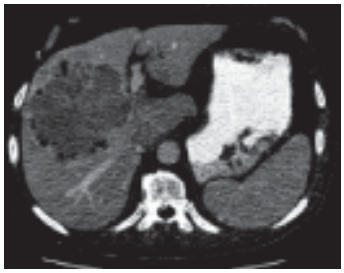

Fig-2d,Wash out in portal venous phase. Note the enhancing capsule.

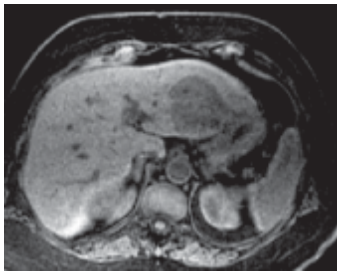

Fig-3a,HCC on T1 WI

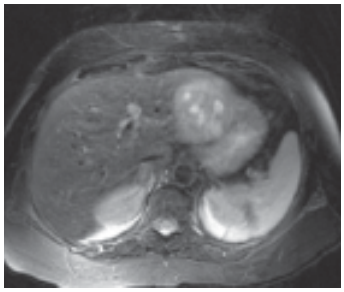

Fig-3b,HCC on T2 WI

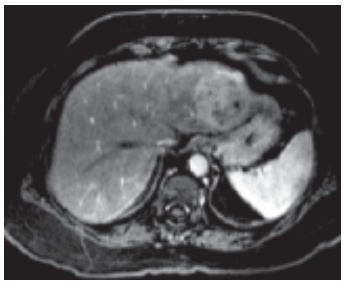

Fig-4a,Dynamic arterial phase – note the enhancement

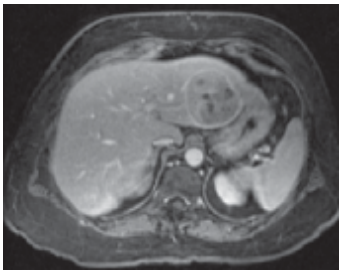

Fig-4b,Wash out on portal venous phase. Note enhancing capsule.

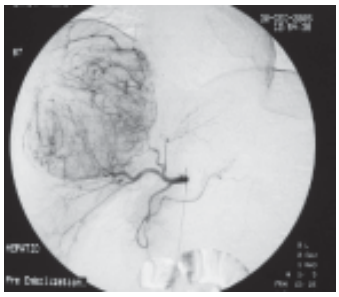

Fig-5a,Pre -embolisation selective arteriogram. Note the hypervascular tumour

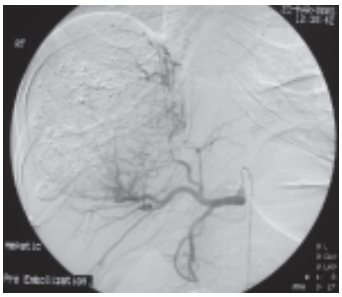

Fig-5b,Post chemoembolisation.

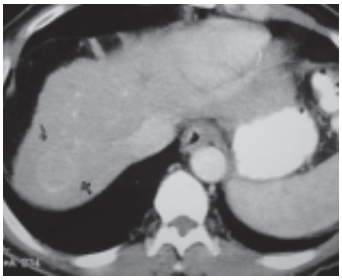

Fig-6a,Rt. Lobe HCC

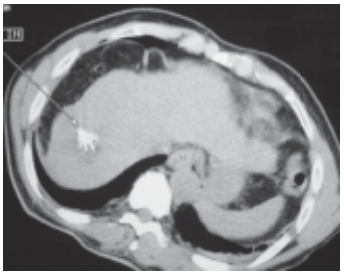

Fig-6b,RF probe deployed in the lesion with prongs open

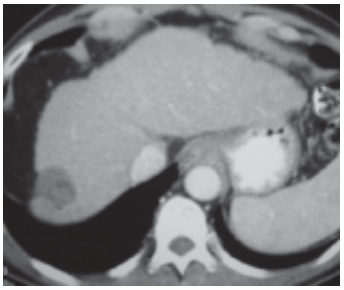

Fig-6c,Follow up CT shows lack of enhancement in the lesion

Surgical in ancient Rome

In the ruins of Pompeii, turned into a time capsule by a volcanic eruption in AD 79, is a house that belonged to a Greek surgeon. It was identified, in 1887, by its large stores of surgical equipment – more than 100 instruments. Since there was relatively little innovation in these tools from the time of Hippocrates in the 5th century BC, instruments like these remained typical of surgical practice for nearly a millennium. In fact, some of them, such as the vaginal speculum, did not change significantly until the 20th century.The instruments found at Pompeii represent the normal range that a surgeon of the time would have needed. They were mostly bronze, brass or copper, but blades and needles were almost invariably made of iron or steel. Most of the instruments could be heated up and used for cautery. By heating the instruments, the surgeons were, without realising it, sterilising them.

Circumcision, scars and brands-The Romans distrusted most of the foreigners they had conquered, and foreigners who wanted to fit in would try to hide telltale differences. That wasn't always easy, especially in the public baths that every respectable Roman visited every day. The Romans, who celebrated the nude body in art and sport, viewed any abnormal appearance of the genitals with distaste, even amusement. The Jews were well known for their insistence on male circumcision, but they were not the only circumcised men known to the Romans. Egyptian priests also practised it, as did Arabs, Ethiopians and Phoenicians.Certain scars were despised. The manly thing was to have battle scars on the front. To have scars on your back was a mark of shame – it showed that you had turned your back in battle and run away or, worse, that you had been whipped – only slaves were whipped. Brands were also hated, as they, too, revealed that you had once been (or still were) a slave, someone who could never enjoy respect.

Importance of Plain Abdominal Radiograph - A Pictorial Essay

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Despite the emergence of superior imaging modalities, the plain abdominal radiograph remains the preferred method of initial radiological examination in patients presenting with acute abdomen. This article discusses the findings in common adult acute abdominal conditions and reviews the role of plain abdominal radiography in the modern scenario.

Radiographic technique-A supine abdomen and an erect chest are the basic standard radiographs [1](Fig-1). A horizontal ray abdominal radiograph, either erect or left lateral decubitus (Fig-2), is frequently taken to demonstrate fluid levels. The erect or decubitus radiographic projections more accurately depict bowel wall and valvulae conniventes thickness.[2](Fig-3). The erect chest radiograph is superior to the erect abdominal radiograph in demonstrating small pneumoperitoneum.

Plain Abdominal Radiograph: Normal Appearance -Relatively large amounts of gas are normally present in the stomach and colon but only a small amount is usually seen in the small bowel. Air and fluid are normal contents of the small bowel, and short fluid levels are not abnormal on an erect radiograph. The amount of gas present in a normal colon is extremely variable, from almost none to what may appear to be abnormal gaseous distension (Fig-4). Sufficient gas is usually present for the colonic haustra to be identified readily. Large bowel caliber is very variable.[1]**Normal small bowel appearances are characterized by** diameter less than 3 cms; wall thickness less than 3mm; fold thickness less than 3mm and three to five air-fluid levels less than 2.5 cm in length, particularly in the right lower quadrant. **Normal large bowel appearances are characterized by** less than 6 cms for transverse colon and less than 9 cms for caecum.

Abnormal Plain Radiograph findings-These include dilatation of bowel; abnormal gas distribution; abnormal bowel wall pattern; inflammatory conditions and abdominal calcification. Let us examine them one by one.

Dilatation of bowel-Gastric dilatation may be due to causes like mechanical gastric outlet obstruction (peptic ulcer, carcinoma), paralytic ileus, gastric volvulus , intubation and air swallowing. Mechanical gastric outlet obstruction leads to a huge fluid-filled stomach that occupies most of the abdomen and is seen on the radiograph as a soft-tissue mass with little or no bowel gas beyond. Gastric volvulus results from twisting of the organ around its long axis (organoaxial) or around its mesentery (mesentericoaxial)[3] (Fig -5A,B). Abnormal intestinal air fluid levels needs to be considered when more than two fluid levels are present in dilated small bowel (caliber greater than 2.5cm) (Fig-6). Small and large bowel obstruction may occur as a) Mechanical obstruction: intrinsic luminal obstruction or extrinsic compression; b) Ileus: severe functional impairment of transit of intestinal contents because of decreased peristaltic activity of the GI tract in the absence of mechanical obstruction and c) Colonic pseudo-obstruction: severe functional impairment of transit of colonic contents and massive dilatation of the colon, in the absence of mechanical obstruction, because of uncoordinated, nonperistaltic, or attenuated colonic muscle contractions.

Mechanical obstruction-Mechanical obstruction can be total or partial. Differentiation between total versus partial obstruction or pseudo-obstruction is critical because the first is generally treated surgically, whereas the latter two are generally treated medically.[4] Mechanical small bowel obstruction causes small-bowel dilatation and a reduction in caliber of large bowel. The amount of gas present in the large bowel depends on the duration of

obstruction and whether obstruction is complete / incomplete. Plain radiograph changes may appear after 3-5 hours if there is complete small bowel obstruction, and are usually marked after 12 hours. With incomplete obstruction, changes on plain radiograph may take days to appear. Plain radiographs are diagnostic in 50% to 70% cases. Radiologic diagnosis requires a dilated, gas-filled proximal bowel and a collapsed gasless distal bowel. A transition zone between dilated and non dilated bowel is a highly specific sign of small bowel obstruction[4]. Unfortunately, this sign is not sensitive. The string of beads sign, due to a line of gas bubbles trapped between the valvulae conniventes, is seen only when very dilated small bowel is almost completely filled with fluid, and is virtually diagnostic of small bowel obstruction [Fig 7A,B].[1] If the plain abdominal radiograph is suggestive of complete small bowel obstruction, further radiological investigations are not necessary, although many surgeons find CT evidence of the likely cause useful. If the plain radiograph suggests partial obstruction and conservative management is contemplated, then the patients are serially monitored clinically and radiologically. Patients who have an uncertain diagnosis of total versus partial mechanical obstruction may prove to have partial obstruction by gradually improving clinically with conservative therapy. Contrariwise, patients initially misdiagnosed with partial obstruction or pseudo-obstruction may manifest radiographic signs of progressive mechanical obstruction.[1]

Closed loop obstruction and strangulation-In closed loop obstruction, a bowel segment is occluded at two points, for e.g. incarcerated hernia, volvulus and colonic obstruction with competent ileocaecal valve. A closed loop obstruction rapidly dilates and is at risk of perforation. In hernia and volvulus, the mesenteric vessels are strangulated leading to bowel ischemia rendering it more prone to complications of necrosis and perforation.If the closed loop is fluid-filled, it may be visible on a radiograph as a soft-tissue mass or pseudotumour. If the loop contains gas, it will be readily visible as a 'coffee bean' shadow. However in many cases, strangulating obstruction may be indistinguishable from simple small bowel obstruction on plain abdominal radiograph. It is important to diagnose closed loop obstruction and strangulation at the earliest because the mortality rises with treatment delay. Hence there is a rationale for performing CT in cases where conservative management is planned to avoid missing strangulation, which would require urgent surgery.[1]

Small vs large bowel dilatation: radiological distinction-In small bowel dilation haustra is absent , the valvulae conniventes is present. The number of loops is many with their distribution of loops centrally located with dimension of loops 3-5cms. The presence of solid feces is the only reliable sign that the loop is large bowel. The other signs can be misleading. Be aware of certain pitfalls. Small bowel fluid levels are by no means specific for obstruction. When severe pain is present anywhere in the body, or when respiration is laboured, the amount of air swallowed is increased, producing gas-filled, slightly dilated loops of bowel with relatively little fluid. The term meteorism is applied to this appearance[1]Radiologically it is difficult to distinguish meteorism from intestinal obstruction but the clinical history and examination enable the radiological findings to be interpreted correctly. Abdominal radiograph can be normal in patients with complete, closed-loop or strangulated obstruction if the bowel loops are fluid-filled.[4] Fluid-filled bowel loops are not readily appreciated on plain radiographs, but are more easily seen on USG and CT

Causes of small bowel obstruction-These include adhesions, hernia, volvulus, ischemic stricture, intussusception, gall stone ileus, foreign body, malrotation and tumor. A hernia may be identified as a gas-filled viscus below the level of the inguinal ligament. Visualization of a hernia does not always mean that it is the cause of the obstruction. If, however a dilated small bowel loop can be identified that points directly to the inguinal region and that also contains a gas shadow in an unusual position, a diagnosis of obstruction due to the hernia can be made

Adynamic ileus-Ileus is an obligatory physiologic response to abdomen surgery [Fig 8]. Duration is related to operative site. Duration is longest after colonic surgery. GI function returns after surgery in an orderly and predictable manner. Small intestinal motility recovers after 0 to 24 hours. Gastric motility recovers by 24 to 48 hours. Colonic motility recovers by 48 to 72 hours.[4]Post operative ileus is prolonged by metabolic derangement, intra-abdominal inflammation and severe infections like pneumonia. Plain abdominal radiograph reveals pronounced small bowel dilatation with lesser degree of colonic dilatation. It is difficult to differentiate post operative ileus from mechanical small bowel obstruction occuring within 30 days of abdominal surgery. Plain radiograph cannot distinguish between them and additional imaging studies are required (contrast studies or CT scan)[4.] Localised ileus is seen in conditions like pancreatitis, appendicitis (sentinel loops)

Large bowel obstruction-LBO is an abdominal emergency associated with high morbidity and significant mortality.The most common cause of LBO is colorectal carcinoma, followed by colonic volvulus and diverticular disease. The clinical presentation varies with the cause. The plain radiographic findings depend on the site of obstruction and competency of ileocaecal valve. In a minority of patients the ileocaecal valve remains competent and, in spite of marked distension of the caecum, the small bowel is not distended. More often, a closed ileo-caecal valve also leads to small bowel distension. In patients with incompetent ileocaecal valve, there may be decompression of the caecum and ascending colon and marked small bowel dilatation.In a review of 140 cases of suspected large bowel obstruction, the plain abdominal radiograph had 84% sensitivity and 72% specificity in diagnosing large bowel obstruction.[4] The plain radiographic appearances of large bowel obstruction are indistinguishable from acute colonic pseudo-obstruction, and any patient with suspected large bowel obstruction therefore requires further imaging (contrast enema or CT scan)

Caecal volvulus[1] **-**It can occur only when the caecum and ascending colon are on a mesentery. In about 50% of cases, the caecum twists and inverts so that the upper pole of caecum and appendix occupy the left upper quadrant. In other cases the twist occurs in an axial plane without inversion and the caecum still occupies the right half of the abdomen. One or two haustral markings are generally seen, even though there is considerable caecal distension (Fig-9). Left side of colon is usually collapsed

Sigmoid volvulus-The radiographic features [3] are ahaustral margin, apex under left hemi diaphragm/above tenth thoracic vertebra, liver overlap sign, left flank overlap sign and pelvis overlap sign (Fig -10).

Acute colonic pseudo-obstruction (ACPO)[4] **-** ACPO is a variant of ileus, characterized by massive colonic dilatation. ACPO can be fatal. It is believed to result from increased sympathetic stimulation or decreased parasympathetic activity. Ogilvie first described this syndrome in 1948 in association with retroperitoneal malignancy infiltrating the celiac plexus. It has been seen in postoperative state, nonoperative trauma, neurologic disease, malignancy, cardiopulmonary disease, intra-abdominal pathology, obstetric disorders and retroperitoneal pathology. Most of the cases spontaneously resolve with conservative therapy. However delayed diagnosis and inappropriate therapy frequently occurs, which results in markedly increased morbidity and mortality. Perforation and colonic ischemia are important complications.Colonic pseudo-obstruction is diagnosed only after excluding mechanical large bowel obstruction. Massive colonic dilatation is present [Fig 11]. An air-filled dilated colon extending distally to the rectosigmoid strongly favors the diagnosis of ACPO rather than large bowel obstruction, but this sign is insensitive. A colonic cut-off point favors the diagnosis of large bowel obstruction; however 40% of patients with ACPO also appear to have a cut-off point. Thus, it is difficult to reliably distinguish between large bowel obstruction and ACPO on plain radiographs alone, hence contrast enemas, CT scan or colonoscopy

are frequently necessary for the diagnosis.

Abnormal Gas Distribution- They are seen as pneumoperitoneum, gas in bowel wall, gas in retroperitoneum and gas in wall of other organs

Pneumoperitoneum- The presence of free gas in the abdomen in the unoperated abdomen almost always indicates hollow viscus perforation. According to Rosco Miller, as little as one ml of free gas can be detected on erect chest film or left lateral decubitus abdominal film. It is also important to recognize the signs of pneumoperitoneum on supine radiographs. These are listed below : a) Visualization of peritoneal surface intra-abdominal organs : bowel – Rigler's sign (Fig-12) and triangle sign, gall bladder sign, inferior liver margin sign (Fig-13) , roof of the bladder ; b) Visualization of surface ligaments as in falciform ligament (Fig-14), football sign, ligamentum teres, gastrocolic ligament, urachus and medial & lateral umbilical ligament (Fig-5); c) Air in intraperitoneal recesses as in Morrison's pouch-doge's cap sign, lesser sac, inferior border of heart and pneumoscrotum; d) Extraluminal gas on liver as in diffusely lucent liver(Fig-16), anterior-superior bubble, ill-defined periduodenal lucency and fissure of ligamentum teres.

Postoperative pneumoperitoneum- Nearly all intraperitoneal air is resorbed by 1 week. Presence of large amounts of air 4-5 days postoperatively should raise suspicion of perforation.

Mimics of pneumoperitoneum- These includes entity like Chiladiti's syndrome, subphrenic abcess, basal atelectasis, subdiaphragmatic fat and pneumatosis intestinalis

Gas in bowel wall - If linear gas streaks are seen in the bowel wall, intestinal infarction should be suspected. Other radiological signs are non specific – slightly dilated loops of small bowel, bowel wall thickening and free gas if perforation has occurred. Pneumatosis cystoids intestinalis is an uncommon condition consisting of cyst-like collections of gas in the walls of hollow viscera.Its aetiology is unknown. The patients do not present with acute abdomen. This condition is mentioned here because occasionally the cysts may rupture, producing a pneumoperitoneum without evidence of peritonitis. Unnecessary laparotomy can be avoided if the characteristic radiographic appearance is recognized.

Gas in retroperitoneum- The causes includes perforation of posterior peptic ulcer, perforated sigmoid diverticular disease, colonoscopy and other iatrogenic causes. Retroperitoneal gas can track superiorly into the mediastinum, and inferiorly into the buttock and thigh.

Gas in wall of other organs- It is due to pneumobilia, portal vein gas, emphysematous pyelonephritis (Fig-17), emphysematous gastritis (Fig-18), emphysematous cholecystitis, emphysematous cystitis (Fig -19) and necrotizing pancreatitis (Fig-20), pancreatic abscess and gangrenous bowel (Fig-21) .

Abnormal bowel wall pattern

Small bowel ischemia is represented by thickening of small bowel wall due to edema and hemorrhage, Gas in the bowel wall. CT scan is far more sensitive.

Large bowel ischemia is featured by 'Thumbprinting' or focal thickening of colonic wall due to submucosal hemorrhage and edema creating an extrinsic impression on the luminal gas (Fig-22).

Inflammatory bowel disease- An assessment of the extent of colitis, the state of the mucosa, the depth of ulceration and the presence / absence of toxic megacolon and perforation can be made. Disease is likely to be inactive where there are formed faeces, while a complete absence of faecal residue suggests extensive colitis. Mucosal changes are outlined by intraluminal gas (Fig-23). When the bowel becomes dilated and the haustra disappear, the ulceration has penetrated the muscle layer and the patient moves in a high-risk group where urgent surgery must be considered. Toxic megacolon is a fulminating form of colitis where the inflammation becomes transmural and ulceration extends deep into the muscle with neuromuscular degeneration. Dilatation of > 5cm represents an initial stage of the process. In established cases the dilatation may be > 8.5 cm. Haustration is always absent, and toxic megacolon should not be diagnosed if it is preserved. Changes are observed mainly in the transverse colon due to the supine position of the patient.

Acute appendicitis-In acute appendicitis, abnormalities are seen in less than 50% of cases. The radiological findings on plain abdominal radiograph are stated below in their relative order of importance. Appendicolith (coprolith, faecolith or appendiceal calculus) – seen in 10-20% of all cases of appendicitis(Fig-24). An appendicolith is formed by precipitation of calcium and phosphate rich mucus around a nidus of inspissated faeces associated with luminal obstruction. Appendicolith and abdominal pain means a 90% probability of appendicitis. The presence of appendicolith indicates a high probability for gangrene/perforation. Approximately 50% of patients with a demonstrable appendicolith will have a perforated appendix at the time of surgery. Children are more likely to have visible calculi. The other findings include sentinel loop – dilated atonic ileum containing a fluid level, dilated caecum, widening of the properitoneal fat line, blurring of the properitoneal fat line, Right lower quadrant haze due to fluid and edema, scoliosis concave to the right, right lower quadrant mass indenting the caecum and blurring of the right psoas outline. All the above findings, with the exception of appendicolith, are non-specific

Acute cholecystitis-This is characterized by Gall stones, Right hypochondrial mass, Duodenal/hepatic flexure ileus and Gas within biliary system

Acute pancreatitis-This is featured by Sentinel loop, Gas filled duodenal cap & loop, Small bowel ileus and Dilated colon particularly transverse and ascending

Abdominal calcification with acute abdomen should alert the radiologist for Gall stones, Limey bile, Appendicolith, Pancreatic calculim, Renal calculi (Fig-25), Ureteric calculi, Calcified aneurysm and Teeth / bone in ovarian dermoid

Conclusion-The plain abdominal radiograph will continue to be the primary radiological investigation in patients with acute abdomen. In certain conditions, the plain radiograph is diagnostic. In some conditions, it provides useful but limited information. Sometimes the findings are nonspecific and further investigations with other modalities are indicated.

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   Medical Clinics of North America 92 (2008)

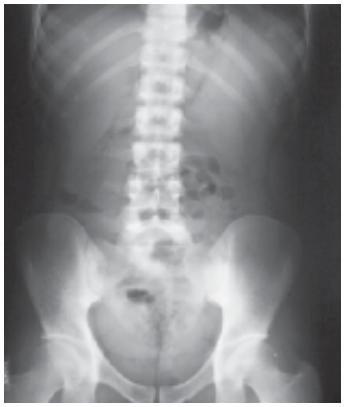


Fig-1: Normal abdominal signature

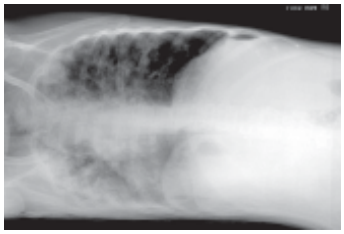


Fig-2 : Left lateral decubitus radiograph taken with horizontal beam shows free gas between the right border of liver and body wall

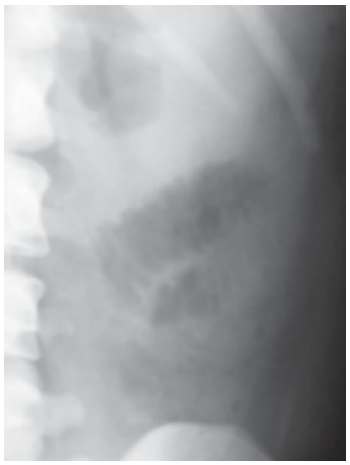
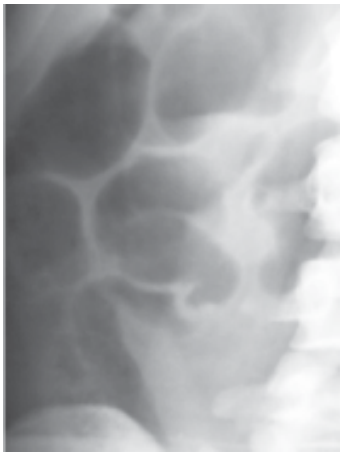
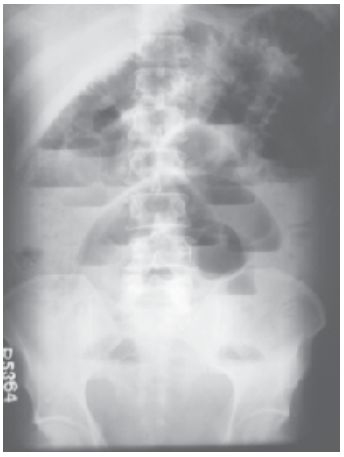


Fig-3 : Normal jejunal loops





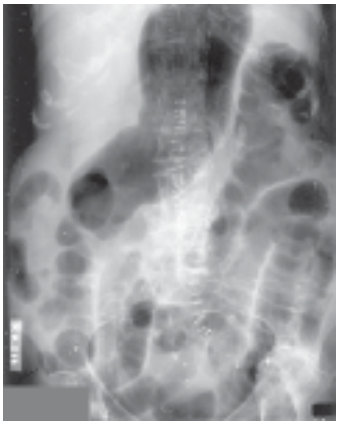


Fig-8: Postoperative ileus: There is pronounced gastric and small bowel dilatation with a lesser degree of colonic dilatation

Fig-6: Complete small bowel obstruction - Multiple dilated small bowel loops with air-fluid levels are seen with little gas in the colon

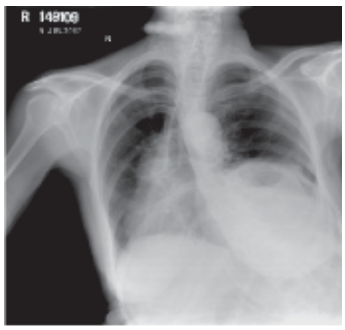


Fig-5 A: Organoaxial volvulus of stomach

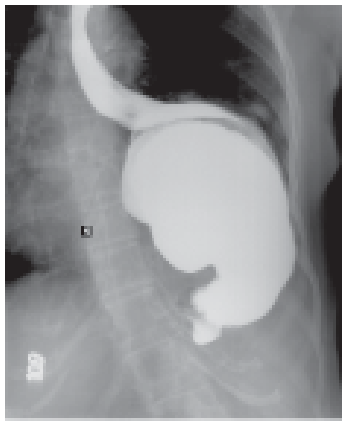


Fig-5B : Organoaxial volvulus of stomach

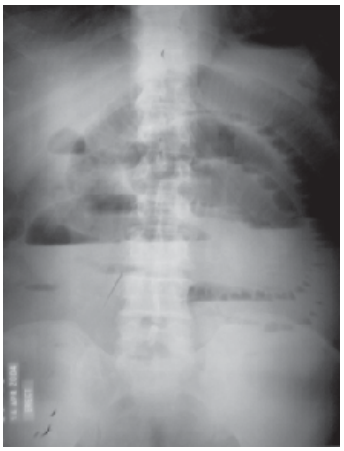


Fig-7B : String of pearls' - diagnostic sign of small bowel obstruction

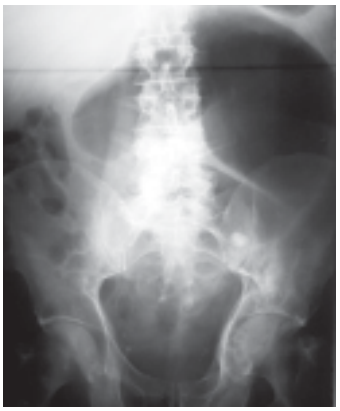


Fig-9 : Caecal volvulus: Convergence of the medial walls of the loop points to the right, a typical finding in caecal volvulus

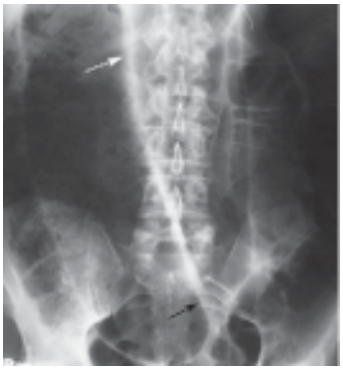


Fig-10 : Sigmoid volvulus: distended ahaustral sigmoid loop (white arrow), inferior convergence of the walls of the sigmoid loop to the left of the midline, and approximation of the medial walls of the sigmoid loop as a summation line (black arrow).

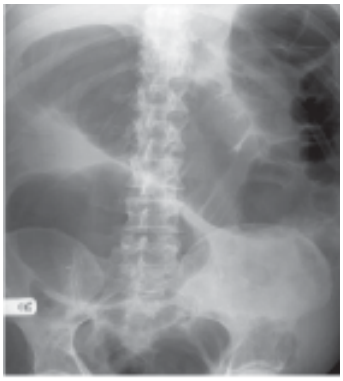
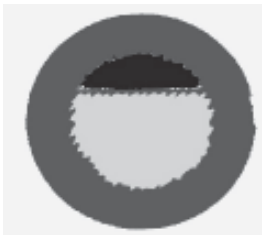


Fig-11:Massive colonic dilatation in a case of acute colonic pseudo- obstruction. The same radiographic appearance can also be produced by mechanical colonic obstruction, toxic megacolon and mesenteric ischemia.

Gas-to-fluid ratio < 1:1

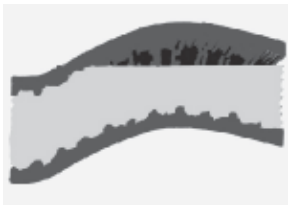
Gas-to-fluid ratio < 1:1

Gas-to-fluid ratio < 1:1

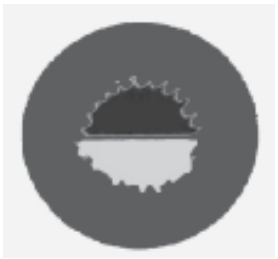


Gas-to-fluid ratio >1:4, best seen on erect film

Gas-to-fluid ratio >1:4, best seen on erect film



Gas-to-fluid ratio >1:4, best seen on erect film



Gas-to-fluid ratio 1:1, same on supine and erect radiographs

Gas-to-fluid ratio 1:1, same on supine and erect radiographs

Gas-to-fluid ratio 1:1, same on supine and erect radiographs

Fig-7A : Varying Gas-to-fluid ratio

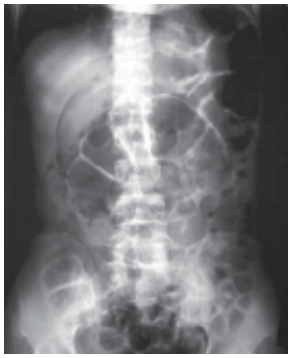


Fig-12: Rigler's sign of pneumoperitoneum: Both sides of the bowel wall can be seen

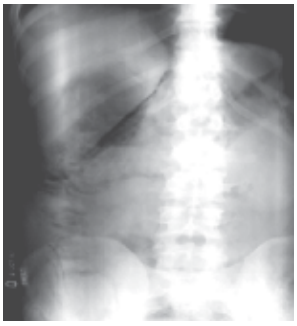


Fig-13: Pneumoperitoneum: In a supine radiograph, free gas collects under the inferior surface of liver ('inferior liver margin' sign)

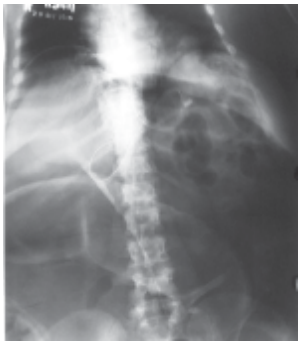


Fig-14: The falciform ligament is outlined by free gas in the abdomen. This sign is seen only when there is large amount of pneumoperitoneum.

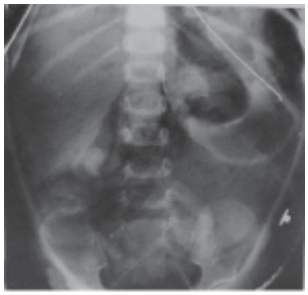


Fig-15: Umbilical ligaments are outlined by pneumopritoneum

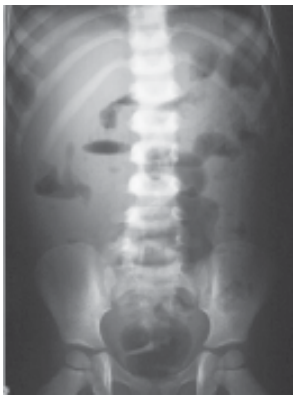


Fig-16: Extraluminal gas is seen over the liver, a sign of pneumoperitoneum on supine radiograph

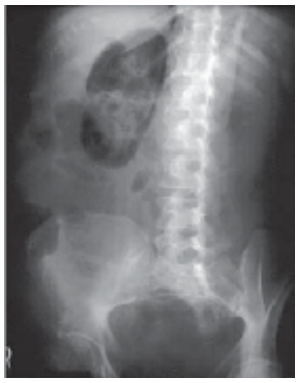


Fig-17: Emphysematous pyelonephritis

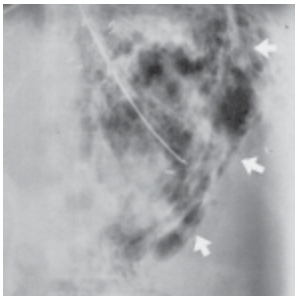


Fig-18: Emphysematous gastritis

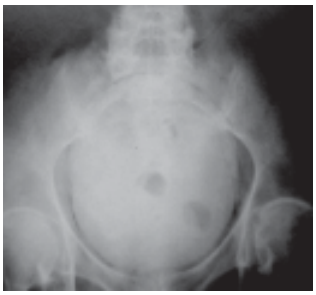


Fig-19: Emphysematous cystitis

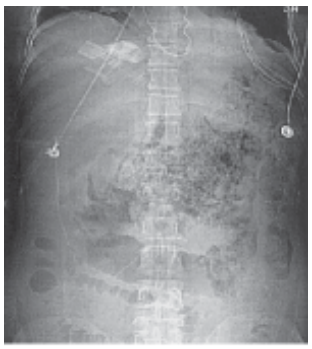


Fig- 20: Necrotising pancreatitis

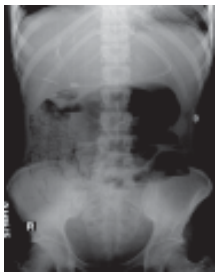


Fig-21: Linear collections of gas are seen in the right colonic wall – Gangrenous bowel was found at surgery

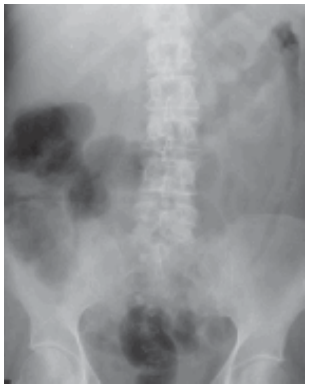


Fig-22: Thumbprinting: focal thickening of colonic wall due to submucosal hemorrhage and edema creating an extrinsic impression on the luminal gas.

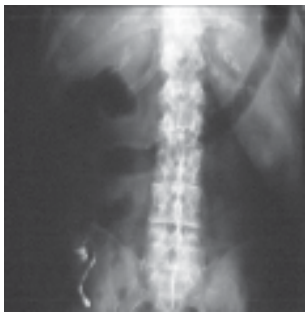


Fig-23: Ulcerative colitis - No faecal residue is seen in the colon. Diffuse luminal narrowing is seen due to spasm

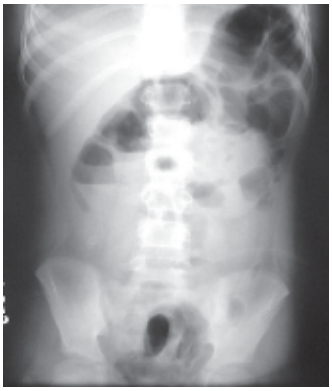


Fig-24: Child with acute abdomen : Appendicolith and abdominal pain means a 90% probability of appendicitis

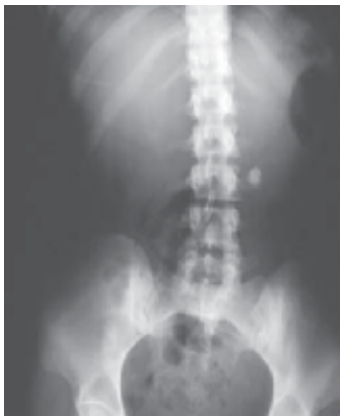


Fig-25: Left renal pelvic calculus

Hippocrates contribution to medicine

Tradition knows seven physicians named Hippocrates, of whom the second is regarded as the most famous. Of his life we know but little. He was born at Cos in 460 or 459 B.C., and died at Larissa about 379. How great his fame was during his lifetime is shown by the fact that Plato compares him with the artists Polycletus and Phidias. Later he was called "the Great" or "the Divine". The historical kernel is probably as follows: a famous physician of this name from Cos flourished in the days of Pericles, and subsequently many things, which his ancestors or his descendants or his school accomplished, were attributed to him as the hero of medical science. The same was true of his writings. What is now known under the title of "Hippocratis Opera" represents the work, not of an individual, but of several persons of different periods and of different schools. It has thus become customary to designate the writings ascribed to Hippocrates by the general title of the "Hippocratic Collection" (Corpus Hippocraticum), and to divide them according to their origin into the works of the schools of Cnidus and of Cos, and of the Sophists. How difficult it is, however, to determine their genuineness is shown that even in the third century before Christ the Alexandrian librarians, who for the first time collected the anonymous scrolls scattered through Hellas, could not reach a definite conclusion. For the development of medical science it is of little consequence who composed the works of the school of Cos for they are more or less permeated by the spirit of one great master. The secret of his immortality rests on the fact that he pointed out the means whereby medicine became a science. His first rule was the observation of individual patients, individualizing in contradistinction to the schematizing of the school of Cnidus. By the observation of all the principles were gradually derived from experience, and these, uniformly arranged, led by induction to a knowledge of the nature of the disease, its course, and its treatment.

9

Review Article

Plain Radiograph in Congenital Heart Disease

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Department of Radiology, Prince Aly Khan Hospital, Mumbai

With the development of echocardiography, radiography now plays an ancillary role in the evaluation of patients suspected to have congenital heart disease. However, sometimes, the chest film provides the first indication of unsuspected cardiovascular disease and in patients with known cardiac disease, radiography offers an important overview of the heart and pulmonary circulation and is useful in follow-up.[1]

Important Caveats-Certain caveats need to be emphasized[1]. Children with relatively mild structural defects and even some with severe or complex disease may have normal chest films. This is particularly true in newborns. Chest radiograph does not usually provide information about specific chamber size, hypertrophy, or intracardiac connections or malformations. Findings such as boot-shaped or egg-shaped heart are nonspecific for tetralogy of Fallot or transposition of the great arteries. On the other hand, plain film findings may be specific for some extracardiac lesions, such as supracardiac total anomalous pulmonary venous return, right aortic arch, pulmonary stenosis and coarctation of aorta.

Systematic evaluation of heart disease on chest film-A systematic evaluation is necessary for successful diagnosis of heart disease on chest film. The following approach advocated by Larry Elliott, is a logical and disciplined method and should be inculcated by all radiology trainees. There are three major stages of analysis[2]. Stage 1 – Extracardiac analysis; Stage 2 – Analysis of pulmonary vascularity ; Stage 3 – Analysis of cardiac anatomy

Stage-1, Extracardiac Analysis

Age-Certain cardiac disorders can be given strong or minimal consideration on age alone. In newborns and infants, ventricular septal defect is the most common, either alone or as part of a more complex process. In older children and teenagers, the lesions with VSD have either been operated upon or have undergone spontaneous closure. Atrial septal defect is the dominant shunt lesion; along with obstructive lesions such as aortic valve stenosis, coarctation of aorta and pulmonary valve stenosis.[2]

Technical Analysis-Alignment – is the patient rotated? It is important because rotation can accentuate normal structures and make them appear abnormal. In infants alignment of medial end of clavicles is not a reliable way to detect rotation. Infants are usually immobilized by holding / strapping their arms and waist. As such the clavicles may be aligned correctly, but the trunk can be so twisted as to result in a rotated thorax. Therefore, the most accurate way to determine proper alignment is to measure the distance between the end of the anterior rib and the lateral margin of the dorsal spine; the right side should equal the left.[2]Films of infants are usually obtained in the anteroposterior and supine positions. Because of the small size of the chest, this technique results in little magnification of the heart, which is a greater issue with larger children. Beam angulation may also affect the appearance of heart and great vessels. With lordotic positioning, the heart may appear more globular, with an uplifted apex and accentuation of the pulmonary outflow tract. With reverse lordosis, much of the heart may be obscured by the hemidiaphragm.[1]Film quality – over or underexposure will affect our judgment of pulmonary vascularity. Ideally, the lungs should appear gray, and the dorsal spine and its interspaces should barely be perceptible through the cardiac shadow. An expiratory radiograph can cause erroneous interpretations of cardiomegaly, shunts and infiltrates. With proper degree of inspiration, the height of the diaphragm should be at the sixth intercostals space anteriorly or the eighth intercostal space posteriorly.

Skeleton-Anomalies of ribs, spine and sternum. For example presence of forked ribs in a cyanotic child -think of Fallot's tetralogy. Bilateral rib notching – coarctation of aorta. Hypersegmented sternum (more than 5 segments), eleven pairs of ribs suggest Down's syndrome, which in turn implies an AV canal lesion. Post surgical stigmata –such as regenerating ribs, unilateral rib notching, surgical sutures and valve / conduit prosthesis.

Abdomen-In every patient, regardless of age, the presence of the liver and spleen should be established.(Fig-1). In asplenia, hepatic symmetry is seen due to enlargement of left lobe of liver. Next, the position of the stomach must be determined. For instance, if the stomach is right-sided in a patient whose thoracic contents appear in the usual position; or is left-sided in a patient whose thoracic contents are in situs inversus, polysplenia syndrome and interruption of the hepatic segment of the inferior vena cava are almost invariably present.[2]

Mediastinum-The last component of stage 1 evaluation concerns structures that are, in reality, not extracardiac. In congenital heart disease, the following have great importance : Position of the aortic arch and Presence or absence of pulmonary trunk

Arch anomalies[2]-The size and position of the trachea is an important indicator of arch abnormalities. A careful search should be made on both frontal and lateral films for displacement or narrowing of the trachea. Right aortic arch can occur as an isolated anomaly or in association with other congenital heart diseases such as tetralogy of Fallot, truncus arteriosus, etc.(Fig-2). Reliable radiographic signs of a right aortic arch are a) absence of the normal aortic knob in the left superior mediastinum; b) indentation and slight deviation of the trachea and c) right-sided descending thoracic aorta. The position and contour of the descending thoracic aorta should be carefully examined. In coarctation of aorta, the only sign in younger children may be a leftward convexity to the descending aorta, which is abnormal in children.

Pulmonary trunk[2]-Presence of pulmonary trunk, regardless of size, allows the following anatomical predictions:a) The great arteries are normally related and connected to the appropriate ventricles; b) There are two ventricles and c) 3. The two ventricles are normally related. In other words, its presence virtually rules out transposition of great arteries and the spectrum of single ventricle entities. This is powerful information usually underutilized by radiologists.

Stage-2, Assessment of pulmonary vascularity : 'Physiologic stage of analysis'

Normal radiographic appearance of pulmonary vasculature-In adults, the main pulmonary artery forms the floor of the pulmonary bay on the frontal chest radiograph. In children and young women, a slight convexity is within normal limits. In the lungs the pulmonary arteries roughly follow the bronchial branching pattern(Fig-3). The arteries branch and taper smoothly out from the hilum and can be followed as discrete shadows to the outer third of the lung. The pulmonary veins of the upper lobe collect into the superior pulmonary vein, those of the lower lobe into the inferior pulmonary vein. The two veins on each side join the four corners of the left atrium. The pulmonary arteries and veins can be distinguished on the plain radiograph by their course and position. The lower lobe veins run horizontally to reach the left atrium and are usually distinguishable from the more vertically running branches of the descending branch of the pulmonary artery. The upper lobe veins, when visible, lie lateral to the upper lobe arteries, and run vertically to pass through the hilar shadow to reach the left atrium. Assessment of the pulmonary circulation is probably the most important observation on the chest radiograph. Analysis of the pulmonary vascularity begins with the central pulmonary arteries and veins (hilar vessels) followed by the intrapulmonary vasculature.

Radiologically normal pulmonary vascularity-It is present in congenital heart disease if the patient is not in heart failure, if no large shunt is present and if there is no extreme pulmonary stenosis. The pulmonary vascularity may look normal on the chest radiograph even in the presence of substantial congenital heart disease.[2]

Increased pulmonary perfusion (plethora)- It is recognized by enlarged central and peripheral pulmonary arteries and veins in all zones. The size of the pulmonary vessels is noticeably larger only when the flow doubles. This means that smaller shunts are not detectable. Detecting moderate increases in flow requires considerable experience(Fig-4). One useful sign is to compare the end-on pulmonary artery to the adjacent bronchus. An arterial diameter greater than that of the bronchus is usually suggestive of increased flow. Another key area is the size of vessels as projected below the diaphragm. When the vessels can be seen this far in the periphery of the lung, it is usually a reliable sign of increased flow.[2] Left – to – right shunts show increased pulmonary vascularity(Fig-5). In cases where the presence of increased vascularity is questionable, analysis of the hilar and intrapulmonary vessels in the lateral and oblique views will often provide the answer. Over a period of time, in patients with significant shunt vascularity, the pulmonary arterioles undergo progressive obliterative changes, the pulmonary vascular resistance steadily increases giving rise to precapillary hypertension. This stage is called Eisenmenger's syndrome (Fig-6). When precapillary hypertension is severe, the following characteristic radiographic appearance is seen. Prominent 'masslike' hilar vessels with diminution in the size of the arteries in the middle and distal third of the lung.[2]

Pulmonary venous hypertension (PVH)-Although shunt lesions are a common cause of prominent hilar and intrapulmonary vessels in children, prominent vascularity secondary to entities creating pulmonary venous hypertension is the most common abnormal vascular pattern encountered; hence a brief discussion is included. The elevated pressure in the pulmonary venous channel is freely transmitted to the pulmonary capillary bed and may be transmitted to the pulmonary arterial system as well. The physiologic and anatomic response of the pulmonary vasculature and lung parenchyma to the effects of PVH are reflected in the chest film as four progressive stages: [2] a) Redistribution of pulmonary blood flow, which involves shunting of blood into the upper lobes and decrease in flow to the lower lobes (the earliest change); b) Interstitial edema which manifests as peribronchial cuffing, Kerley lines ; c) Alveolar edema and d) Chronic changes such as hemosiderin deposits and ossification

Systemic Collateral Arteries - Uncommonly, the pulmonary vasculature appears prominent owing to an increase in flow through the systemic collateral arteries. The usual cause is severe Fallot's tetralogy. Systemic collateral arteries serve as a source of blood supply to the pulmonary arteries. They may originate as bronchial arteries but may take a variety of other forms as well. Their connections with the pulmonary arteries are extremely variable, occurring in the hilum or well into the periphery of the lung. Distinction between prominent pulmonary arteries and veins seen in shunts and systemic collateral arteries is usually not difficult. In the latter, the vessel pattern, although prominent, is disorganized and has a relatively more stringy or reticulated appearance. The prominence is usually nonuniform in the lung or often localized in the direction of the main stem bronchi. This may result in the upper lobe vessels appearing more prominent than the lower. More important, the hilar arteries are not large and are usually inapparent. A normally formed pulmonary trunk is never present.[2]

Decreased pulmonary perfusion (oligaemia)-Decreased pulmonary vascularity nearly always indicates that there is severe obstruction to the flow of blood to the lungs from whichever ventricle the pulmonary artery arises. This may be a morphologic right, left or single ventricle. The obstruction is usually at the pulmonary valve or just below – in the infundibulum – or more commonly at both sites.[2] (Fig-7).When there is diminished pulmonary flow, the hilar and intrapulmonary vessels appear small and the hilar vessels are also less dense than normal. Recognizing this pattern requires considerable experience. The lateral view can be of considerable help in evaluating the size and density of the hilar vessels.

Stage-3, Cardiovascular Anatomy Analysis-The next step is to learn to use anatomical structures within or outside the

cardiac silhouette to determine the level of the shunt. Highly simplified examples are given below. Anomalies that result in pulmonary overcirculation can be divided into those that produce cyanosis and those that don't. From a strict chest-film point of view, acyanotic heart lesions often cannot be distinguished from cyanotic ones.

Acyanotic Congenital Heart Disease-There are four acyanotic lesions that comprise approximately 90% of the shunts encountered – ventricular septal defect (22% to 25%), patent ductus arteriosus (12%), atrial septal defect (8%) and some form of endocardial cushion defect (persistent common atrioventricular canal) (4%)[2]

Radiologic differentiation-There are no specific x-ray signs for a VSD or an ASD. The PDA is the only left-to-right shunt that may show a specific sign. The age of presentation is one of the more important indicators of the type of left-to-right shunt. When there is functional evidence of a left-to-right shunt, the observer must first attempt to determine the level of shunt. The size of the left atrium is valuable in deciding at which level the defect is located and/or the competency of the mitral valve. If in a left-to-right shunt it is found that left atrial enlargement is present, this suggests that the atrial septum is intact and the defect is either at the ventricular or great artery level, or there is, instead, a shunt at any level, with the additional complication of severe mitral valve regurgitation.If, on the other hand, the left atrium is normal in size, this by no means excludes a VSD or PDA. In many infants and almost all children and adults with moderate to large VSD, left atrial size is normal because of closing VSD, development of right ventricular infundibular stenosis or severe pulmonary resistance. In other words, when left atrial enlargement occurs in VSD, it is usually confined to infancy.[2] Following analysis of the left atrium, the second step is an analysis of the aortic arch region for evidence of PDA. A PDA is seen as a convex curvilinear density ('bucket handle' deformity) just below the aortic arch and above the pulmonary trunk. Its morphologic basis is a funnel-shaped widening of the aorta around the opening of the PDA, often termed the infundibulum. In all intracardiac shunts, the aortic arch is often of normal size or inapparent. The right aortic arch has a tendency to occur almost exclusively in VSD than in other left-to-right shunt lesions.In the presence of a left-to-right shunt, absence of left atrial enlargement and a normal aortic arch, together with right heart enlargement, favor a shunt at the atrial level. In children and young adults, the left atrium may enlarge due to mitral incompetence, which, if present, is usually secondary to an incompetent prolapsing mitral valve. In this case, an ASD cannot be distinguished from other shunt lesions causing left atrial enlargement. Although there are no specific x-ray signs for ASD, the diagnosis as well as its exclusion is facilitated by three statistical facts[2] a) ASD (uncomplicated) is rare in infancy; b) the vast majority of shunt lesions in patients older than preschool age ASDs and c) ASD occurs more often in females than other shunt lesions.

Cyanotic Congenital Heart Disease-Among patients with cyanotic heart disease, the vascularity is almost always abnormal (either prominent or diminished).

Cyanotic heart disease – overcirculation vascularity-The conditions include Complete transposition (prototype)(Fig-8); Single or univentricular heart; Tricuspid atresia; Double outlet right ventricle; Truncus arteriosus; Common atrium; Aortic atresia and TAPVC above diaphragm. Statistically, the combination of overcirculation vascularity and cyanosis indicates complete transposition unless proven otherwise. There are no radiologic features pathognomonic for complete transposition.[2] However, certain extracardiac and cardiac findings may indicate another lesion from the above list. For example Skeletal anomalies are commonly seen in truncus arteriosus and common atrium.Presence of right sided aortic arch points towards persistent truncus arteriosus

Cyanotic heart disease with decreased vascularity-These cases can be subdivided into two major groups : a) those associated with a large VSD with the right-

to-left shunt occurring from the ventricle into the aorta and b) those with right-to-left shunt occurring at the atrial level.

Ventricular Level Shunt- Prototype of this group is tetralogy of Fallot. Other conditions are Single ventricle, Tricuspid Atresia, Double outlet right ventricle with severe pulmonary Stenosis, Asplenia syndrome, Corrected transposition with VSD. Roentgenologic findings indicating a large VSD with severe pulmonary stenosis are a prominent aorta with a left aortic arch / (more significantly) right aortic arch; a normal-sized right atrium; a normal sized heart or only mild cardiomegaly. These anatomical findings indicate that the right-to-left shunt is at the ventricular level. With a large VSD, when there is severe obstruction to pulmonary flow, no stimulus for moderate or marked cardiomegaly is present, regardless of the origin of the pulmonary artery, because the ventricles can express themselves easily into the aorta. Moreover, there is usually no tricuspid valve incompetence and thus no stimulus for right atrial enlargement. Extracardiac analysis can help to differentiate some of these conditions. Presence of skeletal anomalies is virtually confined to tetralogy of Fallot. Hepatic symmetry indicates asplenia syndrome.

Atrial Level Shunt-Conditions include Isolated pulmonary stenosis or atresia (prototype); Ebstein's malformation(Fig-9);Tricuspid Atresia; Congenital tricuspid regurgitation; Pericardial effusion and Uhl's anomaly. The major x-ray findings are virtually the opposite of those above and consist of an inapparent aorta; a left aortic arch (right aortic arch is rare); moderate to severe cardiomegaly secondary to right atrial and/or right ventricular dilatation caused by massive tricuspid valve incompetence, which is a coexisting lesion in majority of the above patients. Analysis of extarcardiac and cardiac anatomy can further narrow down the differential diagnosis.

Conclusion-A systematic approach is essential in evaluating chest radiographs in congenital heart disease. In majority of cases the above described approach helps to narrow down to a cardiovascular disease category such as left-to-right shunt or left-sided obstructive lesion, which in turn leads to a differential diagnosis.

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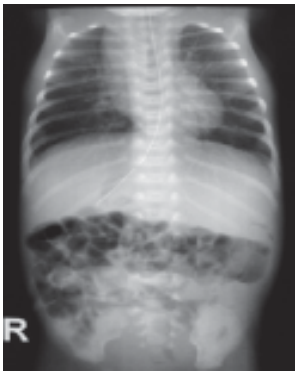


Fig-1 : Extracardiac signs of congenital heart disease Plain radiograph reveals dextrogastria and hepatic symmetry in a neonate suffering from complex cyanotic heart disease. Child also had asplenia and incomplete rotation of intestine (Ivemark syndrome)

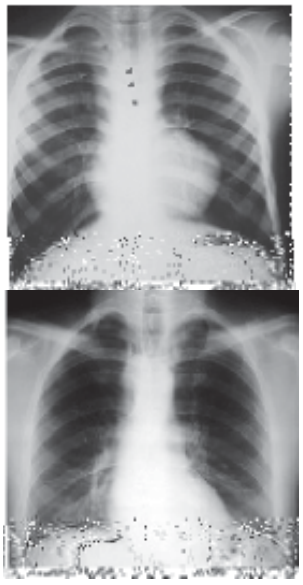
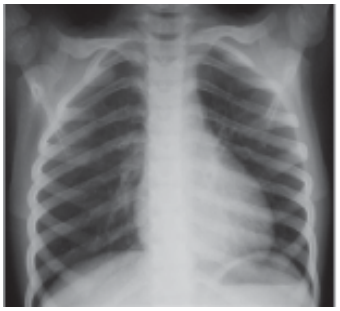


Fig-2 : Extracardiac analysis: Right aortic arch is observed. It may occur as an isolated anomaly or in association with other anomalies like Fallot's tetralogy and persistent truncus arteriosus



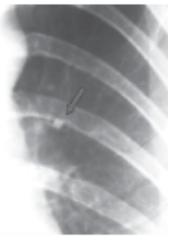


Fig-3 : Normal pulmonary vascularity: The size of pulmonary artery branches normally do not exceed the size of accompanying bronchus

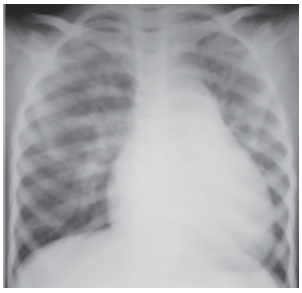


Fig-4: Increased pulmonary vascularity in patent ductus arteriosus

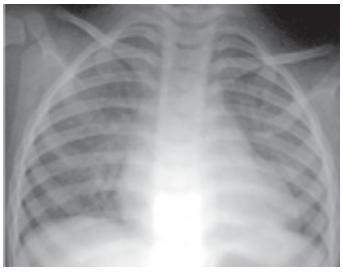


Fig-5 : Analysis in VSD. Pattern of pulmonary vascularity indicates possibility of left-to-right shunt. Child was acyanotic. This patient could have an ASD/VSD/PDA. There are no specific x-ray signs for a VSD or an ASD. The PDA is the only left-to-right shunt that may show a specific sign. The age of presentation is one of the more important indicators of the type of left-to-right shunt

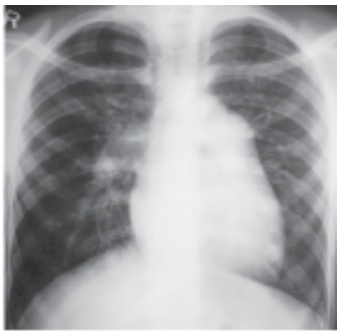


Fig-6 : Eisenmenger's syndrome in a case of ASD: Prominent 'masslike' hilar vessels with diminution in the size of the arteries in the middle and distal third of the lung.

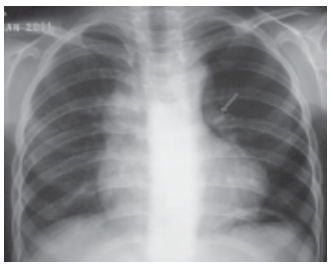


Fig-7: Decreased pulmonary vascularity in Tetralogy of Fallot

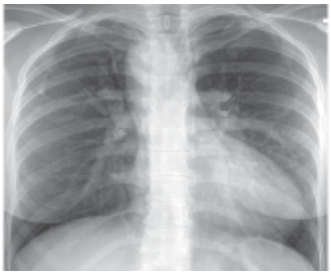
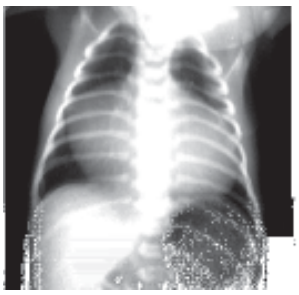


Fig-8 : Patient was cyanotic. Statistically, the combination of overcirculation vascularity and cyanosis indicates complete transposition unless proven otherwise. There are no radiologic features pathognomonic for complete transposition. In this case, the additional finding of right sided aortic arch is highly significant as it strongly suggests persistent truncus arteriosus



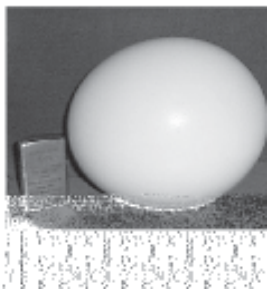


Fig-9 : Egg on Side sign: A case of cyanotic heart disease. There is pulmonary oligaemia, severe right atrial dilatation and an inapparent aorta - a case of Ebstein's malformation

10

Review Article

Gamut of Radiological Findings in Pulmonary Aspergillosis

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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. Aspergillus 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 intracavitary 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 Cytome-galovirus and in malignant conditions like Kaposi's sarcoma and hemorrhagic metastases. The hyphal form of the fungus invades the pulmonary vasculature resulting in pulmo-nary 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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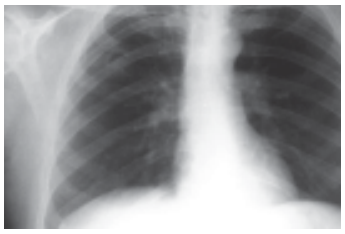

Fig-1,Chest x-ray shows tubular areas of increased opacity in a bronchial distribution and cystic lucencies with opaque cuffs, representing bronchoceles and bronchiectasis respectively.

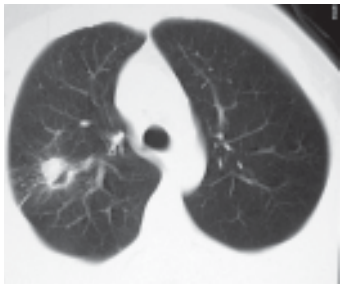

Fig-2,Spiral chest CT shows mucoid impaction (finger-in-glove sign) of dilated bronchi in the right upper lobe.

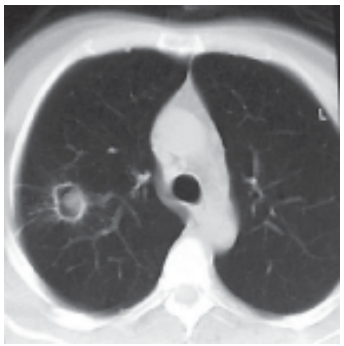

Fig-3, HRCT shows ectatic bronchi with thickened walls filled with hyperdense mucus in the both upper lobes.

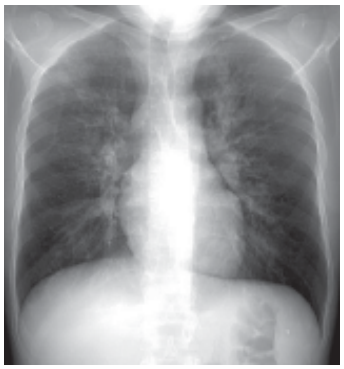

Fig-4, Chest x-ray shows a smooth walled tubercular cavity in the right upper zone with a dependent nodular shadow (fungal ball).

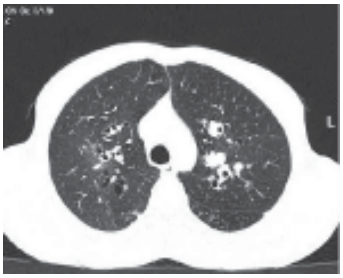

Fig-5, Axial CT scan through the upper chest shows a thin walled cavity in the right upper lobe containing a soft-tissue density mass in contact with the medial wall.

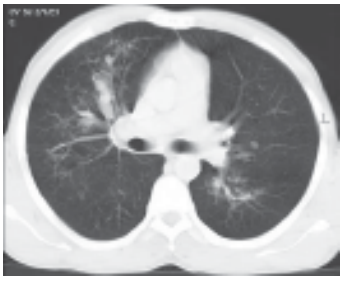

Fig-6,Chest CT with the patient in the right lateral decubitus position shows the fungal ball resting along the lateral wall of the cavity indicating mobility.

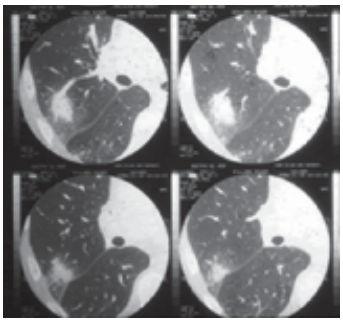

Fig-7,Chest CT shows an irregular airspace opacity in the posterior segment of the right upper lobe (semi-invasive aspergillosis confirmed by FNAC).

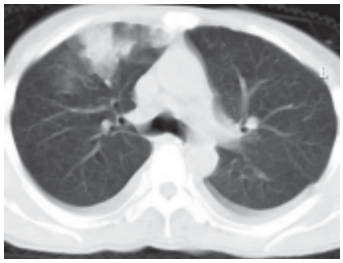

Fig-8, Spiral CT through the upper chest reveals a pleural based wedge shaped infarct in the anterior segment of the right upper lobe.

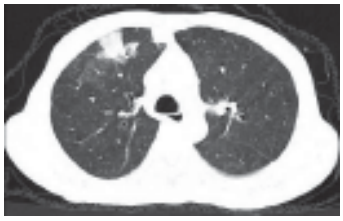

Fig-9, HRCT reveals a halo of ground glass haze surrounding the wedge shaped opacity (infarct)

Medicine in ancient Rome

Alexander the Great had encouraged his physicians to expand the limits of their science, and from the time of Hippocrates, Greek doctors were recognised as the best in the world. The Romans admired them, too, and when they conquered the Greeks in about 100 BC, the physicians were allowed to continue to practise, now as Roman subjects.However, the first Greek doctor/surgeon that the Romans encountered was almost their last. According to the naturalist Pliny the Elder, Arcagathus arrived from Greece in 219 BC. He was made a citizen, and a medical shop was set up for him at state expense. Because he was an expert wound surgeon (*uulnerarius*), he immediately became popular, but this did not last. His enthusiastic use of the knife and cautery – that is, cutting and sealing tissue with high heat – soon earned him the title 'Executioner' (*Carnifex*). More than 100 years elapsed before another Greek physician, Asclepiades of Bithynia, took up residence in Rome.In 46 BC, Julius Caesar granted citizenship to all foreigners teaching a liberal art in Rome. This included the Greek doctors, most of whom were slaves or freed men. When, in 23 BC, Antonius Musa, once Mark Antony's slave, cured the emperor Augustus of a serious illness, he was richly rewarded and won immunity from taxation for all doctors. Later, during the reign of Vespasian (AD 69-79), physicians were also freed from military service.'It's not at all surprising that the Romans used Greek physicians,' says Andrew Wallace-Hadrill, director of the British School at Rome and professor of classics at Reading University. 'Greek medicine was incredibly sophisticated.'The demand for Greek physicians continued to grow, and many Roman cities devised tax incentives to get them to stay. But this was strictly private medicine, with no set pay scale. Only reputation determined prosperity. 'In general, Romans are very superstitious,' continues Wallace-Hadrill, 'and to them the borderline between medicine and magic was very unclear.

11

Review Article

Health System in India

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Health system is a complex of inter related elements that contribute to health in homes, educational institutions, workplace, public places and communities as well as in the physical and psychological environment of an individual and the health and health-related sectors. India is a Union of 35 States/Union territories and being federal nature of constitution of India, States are largely independent in matter relating to health delivery. Each state, therefore, has developed its own system of health care delivery, independent of the central government. The central government responsibility consists mainly of policy making, planning, funding, guiding, assisting, evaluating and coordinating the work of the state health ministries so that health services cover every part of the country and no state lags behind for want of these services. The health care service organizations in the country extend from national to village level.

Central level

The Central Council of Health and Family Welfare was constituted by President under Constitution of India and comprises of Union minister of Health and Family Welfare as chairperson, Minister of state and deputy minister as vice chairperson, member planning commission, minister incharge from the ministry of health and family welfare, Medical education, & public health from the states & Union Territories, member of parliament, eminent person from health and family welfare sector, and senior officials from the Central Government as its member. The council is the apex advisory body and in that capacity considers and recommend broad lines of policy in regard to matters concerning health and family welfare in all aspects; makes proposal for legislation in the field of matter relating to medical, public health and family welfare; examines the whole field of inter-state cooperation;recommends to central government regarding distribution of available grant-in-aid for health and family welfare purpose and reviews periodically the work accomplished and establishes any organization invested with appropriate functions of promoting and maintaining cooperation between the central and state health & family welfare administration. The planning commission and ministry of planning provides over-arching mechanism for policy planning, coordination and implementation. The other official body of the health system at the national level consist of The ministry of Health and Family Welfare; The Directorate General of Health Services.

Union Ministry of Health and Family Welfare-The union ministry of health and family welfare is headed by a cabinet minister, a minister of state and a deputy health minister. These are political appointments. Currently, Union health ministry has following departments Department of Health and Family Welfare; Department of AYUSH [Ayurveda, Yoga & Naturopathy, Unani, Sidha, Homeopathy]; Department of Health Research. Each department is headed by a Secretary to Government of India as its executive head, assisted by joint secretaries, deputy secretaries and a large cadre of administrative staff. In common parlance, it is known as administrative wing of ministry of health and family welfare. The function of the union health ministry have been set out in the seventh schedule of article 246 of the constitution of India under Union list and the concurrent list

Union list-The functions given in the union list are international health relations and administration of port quarantine; administration of central institutes such All India institute of Hygiene and public health, Calcutta; National Institute for the control of Communicable

diseases, Delhi etc.; promotion of research through research institutes and other bodies; regulation and development of medical, pharmaceutical, dental and nursing profession; establishment and maintenance of drug standards; Collection and compilation of census and other statistical data; immigration and emigration; Regulation of labour in the working of mines and oil fields; and coordination with states and other ministries for promotion of health

Concurrent list-The function listed under the concurrent list is responsibility of both the Union and State governments. The centre and the states have simultaneous powers of legislation as may be undertaken by the centre. The concurrent list includes:prevention of extension of communicable disease from one unit to another; prevention of adulteration of food stuffs; control of drug and poisons; vital statistics;labour welfare;ports other than major; Economic and social planning;Population control and family planning

Directorate General of Health Services-The Director General of Health Services is the principal adviser to the Union government in matters relating both to medical and public health. He is assisted by officers of rank of additional director general, a team of deputies and a large number of administrative staff. In common parlance, it is known as the technical wing of ministry of health and family welfare.The general functions are surveys, planning, coordination, programming and appraisal of all health matters in the country. The specific functions are -International health relations and quarantine: All the major ports in the country and international airports are directly controlled by Dte. GHS. All matters relating to obtaining assistance and coordination from international agencies are dealt by Dte.GHS; Control of drug standards: Its primary function is to lay & enforce standards and control the manufacture & distribution of drugs through both central and state government; Medical store depot: These depots supply the civil medical requirements of the central and state governments. These depots also handle supplies from foreign agencies; Post graduate training: Dte.GHS is responsible for administration of national institutes, which also provide post-graduate training to different categories of health personnel; Medical education: As of date, country has 266 medical colleges; Medical Research; Central Government Health Scheme: Health insurance scheme for central government and other employees, parliamentarians etc; National Health Programme; Central Health Education Bureau (CHEB): activities includes development of education material of community and health personnel awareness and training on health education to health personnel; Central Bureau of Health Intelligence (CBHI): collects/collates/compiles, analyze, evaluate and disseminate information on health statistics; National Medical Library [NML] located in New Delhi.

State level-By and large, the organizational structure adopted by the state is in conformity with the pattern of the central government, each headed by a minister and with secretariat under the charge of Secretary/Commissioner [health and family welfare] belonging to the cadre of Indian Administrative Services [IAS]. However, the organizational structure in State directorate of health services is not uniform through out the country e.g. in some states, the programme officers below the rank of Director of health services are called as Additional Director health services while in other states they are called Joint/Deputy director health services. In some states, area of medical education is under the charge of Director medical education and research that is answerable directly to the health Secretary/Commissioner of the state. Some states have created the posts of Director [Ayurveda], and Director [Homeopathy]. Medical care facilities under AYUSH in the country are Ayurveda [2398 hospitals & 13914 dispensaries]; Unani [268 hospitals & 1010 dispensaries]; Siddha [281 hospitals & 464 dispensaries]; Yoga [08 hospitals & 71 dispensaries]; Naturopathy [18 hospitals and 56 dispensaries] and homeopathy [230 hospitals & 5836 dispensaries].

District level-In the recent past, states have reorganized their health services structures in order to bring all health care programs in a district under unified control. This level corresponds to middle level management organization

and is a linkage between the state as well as regional structure on one side and peripheral level structures as CHC, PHC and SC on other side. It receives information from the state level and transmits the same to the periphery by suitable modification to meet the local needs. In doing so, it adopts the function of manager and brings out various issues of general, organizational and administrative types in relation to the management of health services. The district officer with the overall control is designated as the Chief Medical and Health Officer [CM&HO] or the District Medical and Health Officer [DM&HO]. These officers are also known as DMOs or CMOs and are overall incharge of health and family welfare programmes in the district. They are responsible for implementing the programme according to policies laid down and finalized at higher level. Deputy CMOs and programme officers assist these CMOs. Each district usually has a district hospital where most of the specialty services are provided and headed by a officer of a rank of Deputy CMO.

Community health centres [CHC] / Sub divisional hospitals-Community health centres have been established for every 80,000 to 1,20,000 population and this centres was proposed to provide basic specialty services in general medicine, pediatrics, surgery and obstetrics & gynaecology supported by 21 paramedical staff and other staff. The CHCs are established by upgrading the sub-district/taluk hospitals or some of the block level primary health centres or de-novo and are maintained by the state government. According to available information there are 3,910 CHCs in the country.

Primary Health Centre and Subcentre-At present there is one primary health centre covering about 30,000 [20,000 in hilly, desert and difficult terrain's] or more population. Many rural dispensaries have been upgraded to create these PHCs. Each PHCs has one medical officer, two health assistants-one male and one female, health workers and supporting staff i.e. in total there are 14 staff to support medical officer. Under National Rural Health Mission [NRHM], the PHCs have been strengthened by provision of 3 Staff nurse and an AYUSH practitioner. The most peripheral health institutional facility is the subcentre manned by one male and one female multipurpose health worker. According to norms at most places there is one subcentre for about 5000 populations [3,000 in hilly, desert areas and in difficult terrain]. Government of India bears the salary of ANM and health assistant [female]/Lady Health Visitor [LHV] as per state government pay-scale besides rent liability and contingency whereas the salary of male health worker and health assistant [male] is borne by the state government. As on date there are 23,000 PHCs and 1,44,988 subcentres in the country.

Other major agencies providing health care in India Central Government Health Scheme [CGHS]-the scheme was introduced in Delhi on 1st of July, 1954 with the objective to provide health care to the central government employees and members of their families and to do away with the cumbersome and expensive system of reimbursement of medical expenses. The CGHS was initially meant for the central government employees, members and Ex-members of Parliament, judges of supreme-court and high court, freedom fighters and was later extended to people working under various governmental organizations, semi-governmental, semi-autonomous bodies, accredited journalists and ex-governors/ex-vice president of India. As on march 2007, there are 247 allopathic dispensaries, 85 AYUSH dispensaries, 17 polyclinic, 70 labs, 19 dental units in 24 cities for 9 lakh cardholders and 33.01 lakh beneficiaries.

Employee State Insurance Scheme-ESI Act of 1948 and its subsequent amendments, provides for welfare services for employees of industrial, commercial, agricultural and other establishments specified in the act. The scheme has been extended to shops, hotel, restaurants, cinemas including preview theatre, road motor transport undertaking & newspaper establishment employing 20 or more persons. The existing wage limit for coverage under act is Rs. 10,000/- per month [w.e.f. 1.10.2006]. The ESI scheme is being implemented area-wise by stages in all the states except few North-Eastern States. The Employees' State

Insurance Scheme is administered by a Corporate body called the Employees' State Insurance Corporation (ESIC), which has members representing employers, employees, the Central Government, State Governments, medical profes-sion and the Parliament. The Medical care under the Scheme is administered by State Governments, who have the statutory responsibility in this regard, except in Delhi State and Noida area of U.P. Besides, the ESI Hospital, K.K. Nagar at Chennai, ESI Hospital, Thakurpukur at Calcutta and ESI Hospital at Nagda are also being run directly by the Corporation. As per available information [2005], there are 144 ESI hospitals, 42 Annexes, and 1427 dispensaries with 75.70 lakhs registered employees and 329.73 lakhs beneficiaries.

Health-care delivery system in Railways-The objectives of health services of Indian Railways include preventive, promotive and curative health services for its employees/ retired/dependents etc including industrial health; to ensure adequate physical standard of employees and their periodical check-up; to provide and maintain accident relief medical equipment [ARME] including first-aid, to give prompt relief to passengers injured in railway accidents; to attend the passengers taking seriously ill in trains or at railway station; provision of safe food and water supply; ensuring factory and workmen compensation act; certification of death occurring in railway premises and implementation of national health programme programme etc. The apex body in railways health directorate is headed by Director General Railway Health Services at Railway Board, Rail Mantralaya, New Delhi. At Zonal level, there are 16 zonal Railways and each Zonal Railway is headed by one Chief Medical Director (CMD) with Chief Health Directors in some Zones and 2 to 3 Dy.CMDs assisted by few Group 'B' officers. At divisional level, it is mostly headed by Chief Medical Superintendents and in some places Sr. Medical Superintendents are working as in-charge with 2461 general duty medical officers, 45 dental surgeons and 575 visiting specialists. A railway beneficiary receives medical treatment through available Railway health facilities or Govt Hospital or recognized private Hospital. In extreme emergency situation when there is no time for a railway beneficiary to come to Railway hospital then he/she may avail treatment in a private hospital/Government Hospital in the locality and can claim through reimbursement system. There are 121 railway hospitals, 661 health units and 133 approved private institutions for providing specialist care not available in railway hospitals/ health units or nearby other government institution in the country.

Health-care delivery system in Defence-The Armed Forces Medical Services (AFMS), consisting of the Army Medical Corps (AMC), the Army Dental Corps (ADC) and the Military Nursing Services (MNS) provide comprehensive health care to the serving Armed Forces personnel, their families and dependents, numbering approximately 66 lakhs. In addition, Ex-Servicemen and their families are also entitled to free treatment from Services sources as per rules and so are the Para Military Organizations like Assam Rifles, Rashtriya Rifles, Coast Guard as well as the DRDO and Border Road Organization personnel, while posted in the field. Armed Forces Medical Services are also activated in aid to civil authorities during epidemics, natural calamities and internal security duties, especially in inaccessible and difficult areas. In addition to this, life saving emergent care is also provided to all civilians by the establishments of AFMS. Besides the facilities made available in combat zones, 127 hospitals of varying sizes and facilities, spread over the length and breadth of the country, are also functional. While the peripheral hospitals have basic specialist facilities, the eight Command/Army Hospitals have super specialist centers with state-of-the-art equipment and facilities.There is a network of Regimental Aid Posts manned by doctors. These are supported by 89 Field Ambulances, which are mobile 45 bedded hospitals [forward treatment centre] and can organize its medical staff into two Advance Dressing Stations [ADS] and two Medical Aids Posts [MAP]. There are two Field Ambulance Units [FMU] in a division for providing medical cover. The staff of field

ambulance unit comprises of Commanding officer [1], second in command [1], Adjutant [1], surgeon [1], General duty medical officers [6], Non technical officer [1], and other supportive staff.Army medical corps [AMC] provides medical care and other support to the defence personnel and their families through a network of hospitals. AMC also provides for medical manpower to other wings of the defence such as Airforce and the Navy. The post of Director General Armed Forces Medical Services was created in 1949 as coordinating head of the medical services of the Army, Navy and Air Force. The medical units of Airforce include Air force hospitals and Institute of Aerospace Medicine, Banglore for training, aeromedical evaluation and aerospace research.

Private sector and Non-governmental organization-Both formally trained [Allopathy and AYUSH] and *informal [quacks]* players provide basic health services to large proportion of population in the country with 80% share in outpatient and 55% share in inpatient area. These largely include corporate houses, private hospitals, nursing homes, polyclinics, trust/voluntary/ NGO institutions, private practitioners [Trained], and private practitioners [untrained or quacks].

Challenges, issues and concern-The main challenges, issues and concerns are to enhance the allocation of government budget on health sector with simultaneous increase in utilization capacity by different States/UTs; Improving/Enhancing utilization of public health facilities by the community; Regulation of private sector; Maintaining equity, quality of service and focus on 'outcome'; Consolidation and strengthening primary, secondary and tertiary health care for optimal performance and building up appropriate referral services with re-emphasis on primary care; Increasing efficiency, effectiveness, responsiveness and accountability of public health system; Challenge of coordination amongst different organization/bodies and stakeholders for planning and implementation; Community participation.

Ancient medicine in Alexandria

With Alexander the Great's new empire, the West was connected to the East and the South for the first time. The enquiring minds of the Greeks now had access to the rich medical traditions of Egypt and India, of the great physician Skar and of Sushruta, India's first surgeon. Precisely what Alexander's armies brought back from India isn't certain, but all learning, including surgical knowledge, advanced rapidly at about this time. Twenty-three centuries ago, on virgin land on the Mediterranean coast of Egypt, Alexander established his Egyptian capital: Alexandria. After his death in 323 BC, his successor as ruler of Egypt, Ptolemy, was determined to make the city the most important in the Greek world. And as part of this, it became a great centre of science where medicine could flourish. Ptolemy sent agents all over the Greek world to acquire new texts, and visiting ships were obliged by law to leave their manuscripts to be copied. As Alexander himself had wished, a great library was built to house them all. Over half a millennium, it gathered together some 700,000 volumes, including the most comprehensive body of medical texts in ancient history.In addition, the Ptolemy family established a museum – 'house of the Muses' – a publicly funded research institute. Thanks to this and the great library, the development and teaching of scientific knowledge flourished as never before. 'Hippocratic medicine is very interesting,' says Lawrence Bliquez, professor of classics at the University of Washington, 'but with the appearance of *On Medicine* by the Roman writer Celsus [*c.* 25 BC-AD 45], we have much more developed medicine and much more developed surgery. 'What's happened in the meantime? Alexandria has happened. The museum has opened, and the ruling Ptolemy family is very liberal in their support of all sorts of research endeavours – medicine, literature, everything.'For a good 50-year period, we have people such as Herophilus of Chalcedon and Erasistratus of Iulis permitted to perform not only anatomical operations on corpses but also, if we're to believe Galen, vivisection.'

Guidelines on DNB thesis

This is a common observation with most of the assessor selected by the National Board of Examination for thesis/ dissertation that a good large number of dissertations are rejected or sent back for the modification. This article is based on interaction and observations made on these dissertations. This initiative has been taken in order to help the candidates who are selected through a tough All India Entrance Examination and aspire for a better future by passing through the acid test called DNB examination process. This article is also an attempt to caution the guides and supervisors of the candidates who finally sign those theses that are often rejected or sent for modification. Some one has put very rightly ' one has to find out "if the horse is wrong or the rider is wrong or both" before we reject the thesis and blame either the supervisor or the candidate or the both. "Malice ageist non"- is the dictum while composing this article, the very idea is to save the time and energy of the candidate and the supervisor. This is also intended to bring the medical research, especially the clinical research out of its ambiguous state on unreliability to an internationally more acceptable status. The ease to admission through different channels of influences and difficulty in passing the benchmarks that has no reservation or capitation fee facility. The r3equest often comes from these very quarters to raise the pass percentage for these DNB exams! The question often asked is as to why the DNB results are so poor? They should have been better. At the same time we see good results for those who pass out the exams. Here indeed is the need for introspection as to what has gone wrong with our under graduate and postgraduate teaching. Why some candidates from good institutions do well in the theory and viva voce exams while others do not. Is it the defect of the teaching system or the teacher who are often blamed with not doing enough in teaching and education or the reluctant candidate who has known the methods of "cake walk" in the exams when the assessors, examiners were internal as well as the externals are friends of the internal in the viva-voce examination. A favorable situation where more often than not the theory answer sheets are also assessed simultaneously. This is in stark contrast to the DNB exams where you do not even get your own city to appear in the practical viva- voce, what to talk of the examiner being from your own institution or the city .The answer sheets go to four different examiners that are often not connect with Viva-voce. Viewing this entirely different scenario, the assessment is bound to be hard core and not that of facility and felicitation in honor of your own non-performance. The Question I repeat: can the the future of Indian health that is in your hands be left to leniency? Compromising or lowering of the subject knowledge of the students will further aggravate the situation as it is today in terms of health care.

Selection of the topic on the clinical subject- In clinical work the selection of topic should be done after thoroughly studying the feasibility as per the institutional infrastructure and the patient influx. This is purely in order to meet the minimal required criteria of numbers that shall facilitate the statistical analysis.

Synopsis of the thesis-The Synopsis of the thesis: to be shown not only to the committee but also to the assessor to whom the final thesis has to be sent. This will go a long way in preventing the rejection of thesis. This should then be substantiated or supplemented by mid term assessment of the dissertation work that should also be sent to the same assessor.

Candidate - They must have a clear vision so as to why they are there in this course and what are their aims and objectives in order to complete this course: whether to obtain degree so that one gets a job or to get trained in an academic life style that will help the health of the country as well as scientific research based approach in the field of medical sciences.The candidate should also know as to how much is his contribution to Indian statistics as original work or enrichment in pooling high quality genuine data that is inadequate or non-existence on Indian patients. Every project that has to be taken should be done with the view that it shall be sent for publication to a peer reviewed 'indexed journal". Thus in such a situation both the candidate and his supervisor will be benefited and shall devote more efforts in terms of mind , time and dedication to the work. The candidate must refer to several publication available in scientific research such as "How to Write a Paper" or "Scientific Writing- Easy When You know How" by Byword Viva Publishers 4262/3 Ansari Road, Darya Ganj New Delhi 110002) and get his / her life style modified in scientific approach while working for the dissertation. There are such several other publications to guide the dissertation work.The cut and paste culture: a good large number of theses are coming that are cut and past from the website. I am remained of professor of pathology who came across one thesis that was totally cut and paste from websites and there was no bibliography in that thesis. There are cases where the whole thesis has been copied from some body else's M.D. or DNB probably with a self assurance that the assessor shall not know about it. Yet in another case the idea and subject of the thesis was great but the institution neither had infra structure or expertise to carry it out and hence total fabrication. In most cases it may not be possible to detect but this is not going to help the candidate. There are examples of such fraudulent work since time immemorial when a candidate had produces a thesis on hyperthermia when the equipment to give the same was non-existent in Northern part of the country. Or when the candidate has produced a thesis when his department was shut down by AERB during the tuner of his thesis. Sooner or later the stories leak out and may cause embarrassment to the candidate.

Review of literature - In general the candidates have habit of quoting western epidemiological data fresh from Europe , America and Japan that has little relevance in dealing with the Indian population. At least in case of Oncological Sciences we have national Cancer Registry of ICMR that is able to provide a great deal from their metropolitan and hospital based tumor registries. Other specializations should be having similar registries to be embarked upon. If not it is high time that it is created.

Randomization in clinical subjects like oncology- Before starting the thesis the candidate must understand the tenets of scientific research and the trials. The whole project or the protocol needs to be shown to the bio statistician of some experience before the work is started. This will give a proper directives for the selection for the topic and the minimal desirable number of cases that candidate has to complete during the training tenure. It is nice to work on the rarest of the rare disease but it should be carried out with adequate number that shall enable it for statistical analysis. It is here the strict stance that is require in the preparation of dissertation that shall lead to emergence of realistic data on Indian patients. This shall give a chance to compare the Indian data versus oft-repeated quotations from western epidemiological data that has no relevance to Indian scenario with regards to the solution, prevention and control of the disease. There should be proper utilization of tools to represent the observation such as tabulation, bar diagrammes histograms etc. It is always better to follow a standard format of thesis writing rather than creating one's own. Title Page, Certifications, Forwards, Words of Gratitude, Index, Abbreviations, Introduction, Aims & Objectives Review of Literature, Material and Methods, Observation, Discussion, Conclusion, Bibliography/refer-

ences, Annexure, Master chart etc.

Institutions-The institutions should equip themselves to carry out these high profile scientific works required for the future and career of the candidate. The institution should not only provide the proper minimal infrastructure and staff but should also provide time to the candidates for his studies and work, not using them as cheap labor for routine work or to appease the employers by enhance the earning from patient treatment or private practice.The bio statistician, the dietician, the medical physicist, the physio-therapist etc. the paramedical facilities should be provided so that the work is carried out in a proper manner. Indeed it is in good favor of the institution if good quality research work is published in journals of international repute exemplifying the genuineness and sincerity behind the work. This should form a national phenomenon from every institution conduction DNB courses. Instead of only few institutions being favored for the acceptance of publications just because of the reasons such as esteemed nametag attached to them, high quality contribution from every institution should become the usual happening.

Guide-One should not forget the stark reality that the career making means good number of publications in indexed and peer reviewed journals. One should also not forget the fact that with the modern information technology tools available the scrutiny and surveillance by the peer reviewed indexed journals is becoming stricter, day by day. In such a situation the work carried out should be supervised in such a manner that it stands the acid test of the standards observed by these journals. At any point of time the DNB dissertation work should not be taken lightly as it concerns the candidates future who is the future health care provider of the country as well as for the patients life or for that mater the medical sciences research in India. The guide should have bimonthly review of the candidate's work and just not sign the thesis at the fag end of the work , at times without going through the draft even!!. Guide should also keep in touch with the NBE in order to appraise the board about the progress of the candidate. The NBE shall have to equip itself for the same. Though to the candidate and to the NBE this may cost a little extra in terms of time and money and man power but it shall certainly improve the standards and solve certain big looking trivial problems. The guide himself has to train himself and apprise himself with the basic tenets of medical and clinical research because many a these thesis have given similar signals that the guides lacked scientific temperament and they themselves were not been founded firmly on fundamentals of the medical research and training work. This is the most desired change that the guides have to bring about in themselves that the institutions that are approved for DNB courses need not remain the commercial health complex but also serve as useful centers for serious scientific research too. The guides have to develop a scientific temperament and the prime aim and objective for the DNB candidate should be his research and clinical/ academic training and not the easy, vulnerable manpower to serve and run that institution's day to day affairs.The Midterm assessment of the thesis work and modification thereby-The best way to avoid this malady is to have a mid term assessment of the dissertation work. This should be done locally by the guide and his departmental research committee and then should be sent to the same expert who is also going to assess the thesis finally.This shall prevent the situation like thesis coming for the modification when the candidate has finished his tenure in the institution.

What should candidate and his guide do if the thesis comes for modification after the tenure is completed?-First thing they should remember that the medical life is never ending learning and so is the medical research. The time restraints for the course in full view the candidate should not wind up the work, instead continue the work till the end of the tenure . This means that the candidate is provide another six months to harvest the cases in order to

fortify his statistical pool; institution and candidate gets an additional follow up data; the continuation of the project may add to institutional long term study that can be utilized by another candidate for further observation .They should not forget to send the work report in mid term to the assessor whosoever he may be through NBE so that directives or modification if at all can be communicated. Candidate should collected sufficient date with probability of off shoots of the work. Should follow the basic tenets of the scientific research in first place so that the thesis does not stand the risk of rejection or modification.The Guide should have "on going projects" with a wider scope and aims and objectives so that in case of the diseases that do not provide sufficient number of patients, a better pooling of data is made available to the candidate in form of a retrospective and prospective study.

What should candidate and the institution do if the guide goes away!-From the very beginning the Institutional administration should allocate a standby guide who can supervise in case of demise or abstention of the actual guide of the candidate. Some kind of co-guide or sub guide. This should be possible in the institutions where there is rapid rate of exit and entry of the consultants as one sees in private five star institutions.

Is dissertation just a passport to DNB Degree?-he Issue is not that the candidate has passed the theory and practical examination so he is eligible for the degree. In that case there is no need for the dissertation of thesis. The question is that the making of a specialist should be based on the firm footing of scientific research , the process of the learning of medical science. The purpose of dissertation is to create a new generation of medical scientist who can contribute genuine – non fraudulent, non copycat data to the pool of Indian scientific data. The purpose is to shun or discourage the fictitious / hijacked or stolen work that is a common practice in many of the institutions. Instead of the candidate undergoing the rigmaroles and grooving for the whole tenure of the course that is meant to make him a genuine scientist,the thesis from the premier institutions or the departments that have a national or international repute are copied in-toto and are sent as dissertation and that takes few days time in making it . The purpose of strict standards in the dissertation is to correct the wrong impression of the peer reviewed index journal and their editorial board that rejects such articles and often accept the articles blindfoldedly, when it comes from some handful of so called premier institutions of India - irrespective of the fact that in that scientific publication churning industry many of the publications there too are far below standards , statistics stage managed like tables of number..... 2, 2za 4 and 4, 4za 16 .Referring to the Guides on Scientific paper making or research procedures-The literature available in these books that give directives on trials and scientific paper publications will certainly improve the quality of Indian medical research especially so on the clinical and para-clinical side and the credit thus has to go to National Board that has with its untiring efforts has set a bench mark not only in the realm of post graduate education but also in the realm of medical sciences research. An area that needs serious reformation and image building in front of international players from the developed countries. In a recent experience it was found that the candidates have complained as to why the results in the DNB examination are so poor from their state- 10 percent only ! It is apparently the combine or the net result of all the success and failures inclusive of dissertation, theory paper and practical viva-voce and one has to reform oneself at every step of this tenure and programme.

Suggestions to tackling this problem - There are audio visual aids provided in form of CDs,IGNOU programmes on various topics through Gyan Darshan and Gyan Vanee channels. And the candidates must watch these programmes related to their subjects as well as the associated subjects.The broadcast/ telecast schedule is put on the NBE web site and

newsletters.Secondly the CMEs that are arranged by NBE on various topics. The student should also attend the CMEs conducted by the scientific body of their specialty and for that the Institutions should give all the possible help to the candidates to attend these CMEs.The best suggestion that has come from the crowd of the students themselves is to form a scientific Association of DNB candidates. Under the auspices of the same association regular conferences and seminars to be held on methods of reforming the education and training of the candidates. There has to be the interactive sessions with the experts, the examiners and the administrators in the NBE so that they can put their view point and the candidates and their guides can put their view point. Although a stupendous job, this will help in a long term manner those hundreds of thousands of aspiring young candidates who want to become specialists and super specialist. The Institutions that are already contributing their might to conduct DNB sponsored CMEs should take the responsibility to arrange such Zonal Conferences of Association of DNB Candidates.

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History of treatment of Aneurysm

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.

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".

13

Recent Advances

Sugammadex- a novel neuromuscular blocker binding agent – a Review

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Steroidal neuromuscular blocking agents (NMBD), such as rocuronium, are widely used in clinical anesthesia and emergency medicine to facilitate tracheal intubation and artificial ventilation[1]. Reversal of neuromuscular blockade is important for the acceleration of patient recovery and prevention of postoperative residual neuromuscular blockade[1,2,3]. Currently, the reversal of neuromuscular blockade is achieved by the administration of acetylcholinesterase inhibitors (neostigmine, edrophonium, or pyridostigmine)[1]. Acetylcholinesterase inhibitors, however, have some problems with their use[4]. Early or "escape" reversal after a short case or an unexpected cannot intubate, cannot-ventilate scenario using neostigmine is limited[4,5]. The inability of cholinesterase inhibitors to reverse a profound nondepolarizing blockade may be one important reason for the unrelenting persistence of succinylcholine in current anesthetic practice, in particular for its two principal indications, relaxation for rapid sequence induction and ultrashort procedures[5]. In addition, acetylcholinesterase inhibitors have effects associated with stimulation of the muscarinic receptors resulting in bradycardia, arrhythmias, increased secretions and contraction of smooth muscle, though these can be counteracted by coadministration of muscarinic antagonists (atropine or glycopyrrolate)[1,4,6,7]. However, muscarinic antagonists also have side effects (blurred vision, dry mouth, and tachycardia)[1]. Few studies have attempted to explore the potential of nonclassic reversal drugs[8]. In this regard, suramin, a P_2-purinoceptor antagonist, can reverse nondepolarizing neuromuscular blockade , but it has serious side effects that render it inapplicable for routine clinical use[8].In contrast, purified human plasma cholinesterase has been shown to be an effective and safe drug in antagonizing mivacurium-induced neuromuscular blockade[8]. Similarly, cysteine has been shown to reverse the neuromuscular blocking effects of gantacurium. Notably, both purified human plasma cholinesterase and cysteine act independently of acetylcholinesterase inhibition[8].

There is thus a clear need for new reversal agents with a rapid onset of action and an improved efficacy and safety profile.and having the capability to reverse neuromuscular blockade effectively, independently of its depth.

Suggamadex-A novel approach to reversing neuromuscular blockade is sugammadex (Org 25969) (Su refers to sugar and gammadex refers to the structural molecule-gamma-cyclodextrin), a selective relaxant binding agent (SRBD), made up of a ring of eight sugars, to which negatively charged side chains were added for the purpose of binding rocuronium and other steroid-based neuromuscular blocking agents[8,9,10].

Mechanism of Action- Sugammadex is inert chemically and does not bind to any receptor. It acts by rapidly encapsulating steroidal NMBDs to form a stable complex at a 1:1 ratio and thus decreasing the free concentration of the drug from the plasma[1,8,10,11,12,16]. This creates a concentration gradient favoring the movement of the remaining rocuronium molecules from the neuromuscular junction back into the plasma, where they are encapsulated by free sugammadex molecules. The latter molecules also enter the tissues and form a complex with rocuronium. Therefore, the neuromuscular blockade of rocuronium is terminated rapidly by the diffusion of rocuronium away from the neuromuscular junction back into the plasma[8].

Chemical structure-NMBD are quaternary ammonium compounds with at least one charged nitrogen atom. Cyclodextrins have a lipophilic centre but a hydrophilic outer core, attributable to negatively charged ions on their surface. These negatively

charged ions on the surface of sugammadex attract the positive charges of the quaternary ammonium relaxant, drawing the drug in to the central core of the cyclodextrin[13]. The binding of the guest molecule into the host cyclodextrin occurs because of van der Waal's forces, hydrophobic and electrostatic interactions. The structure of the cyclodextrin is such that all four hydrophobic rings of the steroidal relaxant fit tightly within the concentric doughnut forming an inclusion complex. This has been confirmed by calorimetry and X-ray crystallography[13]. Such a reaction occurs in the plasma—not at the neuromuscular junction—and the concentration of free rocuronium in the plasma decrease rapidly after sugammadex administration[13].

Pharmacokinetics-The encapsulated complex of sugammadex and NMBD are freely filtered by the glomerulus into the urine. The plasma clearance of the complex is the same as the glomerular filtration rate (120 ml/min)[13]. No dissociation of this tightly knit complex occurs in the plasma.

The main difference in the pharmacokinetic profile of sugammadex and rocuronium is that the clearance of sugammadex is approximately three times lower than that of rocuronium[5]. In the absence of sugammadex, rocuronium is eliminated mainly by excretion into bile and feces. In the presence of sugammadex, however, urinary excretion of the rocuronium–sugammadex complex is the major route of elimination of rocuronium[5,7]. Interestingly, shortly after administration of sugammadex, the total plasma concentration of rocuronium increases. This can be explained by redistribution of free rocuronium from the peripheral compartments back to plasma as a result of the decreased free plasma concentration[5]. Redistributed free rocuronium is largely encapsulated by sugammadex, thus increasing the total rocuronium concentration.

Suggamadex and investigation trials-Sacen et al [6] did their study on 60 patients undergoing elective surgery with a desflurane–remifentanil–rocuronium anesthetic technique who received either sugammadex, 4 mg/kg IV, edrophonium, 1 mg/kg IV and atropine, 10 mg/kg IV, or neostigmine, 70 mg/kg IV and glycopyrrolate, 14 mg/kg IV for reversal of neuromuscular blockade at 15 min or longer after the last dose of rocuronium using train-of-four (TOF) responses. They found that although the initial twitch heights (T_1) at the time of reversal were similar in all three groups, the time to achieve TOF ratios of 0.7 and 0.9 were significantly shorter with sugammadex (71 ± 25 and 107 ± 61 s) than edrophonium (202 ±171 and 331 ± 27 s) or neostigmine (625 ± 341 and 1044 ±590 s). All patients in the sugammadex group achieved a TOF ratio of 0.9 d"5 min after reversal administration compared with none and 5% in the edrophonium and neostigmine groups, respectively. They concluded that Sugammadex, 4 mg/kg IV, more rapidly and effectively reversed residual neuromuscular blockade when compared with neostigmine (70 mg/kg IV) and edrophonium (1 mg/kg IV). In contrast to Sorgenfrei et al.[7], they found no evidence of a hypotensive effect due to sugammadex when it was administered under steady-state anesthetic conditions[6].In contrast to propofol, sevoflurane enhances the effects of some NMBDs, including rocuronium[10]. Xue et al[14], Kim et al [15] showed that sevoflurane can significantly prolong the duration of action of rocuronium and the time to recovery. These effects are not seen with either propofol or isoflurane. Vanacker et al[10] investigated whether sugammadex, is equally effective at reversing rocuronium-induced neuromuscular block in patients under propofol or sevoflurane anesthesia. After receiving propofol for induction, patients were randomized to propofol (n = 21) or sevoflurane (n = 21). Rocuronium 0.6 mg/kg was administered for tracheal intubation. At reappearance of the second twitch of the TOF ratio, sugammadex 2.0 mg/kg was administered. Mean recovery time for recovery of train-of-four ratio to 0.9 was 1.8 min after both propofol and sevoflurane anesthesia. Sugammadex is reported to be effective and well tolerated in healthy volunteers and surgical patients at doses up to 16.0 mg/kg[11]. Additionally, sugammadex at doses of 2.0–4.0 mg/kg has been shown to safely reverse moderate neuromuscular block induced by rocuronium in a

dose-dependent manner. Groudine et al[11] enrolled 50 patients into a Phase II dose-finding study of the efficacy and safety of sugammadex. Subjects, anesthetized with nitrous oxide and propofol, were randomized to one of two doses of rocuronium (0.6 or 1.2 mg/kg) and to one of five doses of sugammadex (0.5, 1.0, 2.0, 4.0 or 8.0 mg/kg). Sugammadex was administered during profound block when neuromuscular monitoring demonstrated a posttetanic count of one or two. They concluded that the mean time to recovery decreased with increasing doses. Sugammadex doses of1.0 mg/kg did not bind sufficient rocuronium to rapidly reverse a profound NMB. Doses e"2 mg/kg of sugammadex consistently resulted in a TOF ratio e"0.9 in 15 min or less. Increasing the dose from this level resulted in faster reversal[11].This may indicate that sugammadexat doses of 0.5–1.0 mg/kg does not reliably bind sufficient rocuronium to produce complete reversal of the NMBD[17]. A molecule of sugammadex (molecular weight 2178) is approximately 3.6 times heavier than a molecule of rocuronium (molecular weight 610)[11]. This would suggest that a dose of 1.8 mg/kg of sugammadex would be required bind all the rocuronium in a 0.5 mg/kg dose[11]. Boer et al[1] investigated the efficacy and safety of sugammadex in reversing rocuronium-induced profound neuromuscular blockade at 5 min in 45 patients. Anesthesia was induced and maintained with propofol and an opioid. Profound neuromuscular blockade was induced with 1.2 mg/kg rocuronium bromide. Sugammadex (2.0, 4.0, 8.0, 12.0, or 16.0 mg/kg) or placebo (0.9% saline) was then administered 5 min after the administration of rocuronium. They concluded that increasing doses of sugammadex reduced the mean recovery time from 122 min (spontaneous recovery) to less than 2 min in a dose-dependent manner. This study showed that, compared with spontaneous recovery, sugammadex produces rapid and effective reversal of profound rocuronium-induced neuromuscular blockade, without signs of residual or recurrence of neuromuscular blockade. Increasing the dose of sugammadex up to 16 mg/kg reduced the mean recovery time to a TOF ratio of 0.9 from 122.1 min (spontaneous recovery to less than 2 min). A clear dose–response relation between the time from start of administration of sugammadex and recovery of the TOF ratio to 0.9 was seen[1]. Suy et al[16] explored the dose–response relation of sugammadex rocuronium (0.60 mg/kg) and vecuronium (0.1 mg/kg) in 80 patients. Compared with placebo, sugammadex produced dose-dependent decreases in mean time to recovery for all train-of-four ratios in the rocuronium and vecuronium groups. The mean time for recovery of the TOF ratio to 0.9 in the rocuronium group was 31.8 min after placebo compared with 3.7 and 1.1 min after 0.5 and 4.0 mg/kg sugammadex, respectively. The mean time for recovery of the train-of-four ratio to 0.9 in the vecuronium group was 48.8 min after placebo, compared with 2.5 and 1.4 min after 1.0 and 8.0 mg/kg sugammadex, respectively. They concluded *sugammadex* rapidly reversed rocuronium- or vecuronium-induced neuromuscular block at reappearance of the second muscle twitch. A dose–response relation was observed with sugammadex for reversal of both rocuronium- and vecuronium-induced neuromuscular block.Sorgenfrei[7] investigated 27 subjects, randomized to receive placebo or sugammadex (0.5, 1.0, 2.0, 3.0, or 4.0 mg/kg) for reversal of 0.6 mg/kg rocuronium– induced neuromuscular block. Anesthesia was induced and maintained using intravenous fentanyl and propofol.. Sugammadex or placebo was administered at reappearance of T_2 of the TOF. Sugammadex decreased median recovery time in a dose-dependent manner from 21.0 min in the placebo group to 1.1 min in the group receiving 4.0 mg/kg sugammadex. Doses of sugammadex of 2.0 mg/kg or greater reversed rocuronium induced neuromuscular block within 3 min. A median of 59–77% of sugammadex was excreted unchanged in the urine within 16 hr, mostly in the first 8hr. Sugammadex increased the proportion of the rocuronium dose excreted unchanged in the urine (from a median of 19% in the placebo group to 53% in the 4.0-mg/kg group within 16 h). No evidence of recurarization was observed in any patient. They concluded that at doses of 2.0 mg/kg or greater, sugammadex

safely reversed 0.6 mg/kg rocuronium–induced neuromuscular block in a dose-dependent manner. Sugammadex enhanced renal excretion of rocuronium and was excreted unchanged by the kidneys.While sugammadex appears to be superior and an outstanding SRBA, the case report by Eleveld et al.[17] reminds us that all drugs have a dose–response type of pharmacology. They administered a very small dose of sugammadex (0.5 mg/kg) for a rocuronium neuromuscular block (0.9 mg/kg). Although reversal was initially successful, the neuromuscular block partially reappeared[18]. Cammu et al[12] investigated the single i.v. doses of sugammadex 16, 20, or 32 mg/ kg administered simultaneously with 1.2 mg/kg rocuronium or 0.1 mg/kg vecuronium to 12 anaesthetized (with propofol/remifentanil) and non-anaesthetized healthy volunteers. They found, rocuronium/ vecuronium plasma concentrations declined faster than those of sugammadex. They concluded that single-dose administration of sugammadex 16, 20, or 32 mg/kg in combination with rocuronium 1.2 mg/kg or vecuronium 0.1 mg/ kg was well tolerated with no clinical evidence of residual neuromuscular block, confirming that these combinations can safely be administered simultaneously to non-anaesthetized subjects. Shields et al[4] studied 30 anaesthetized patients who received rocuronium 0.6 mg/kg as an initial dose followed by increments to maintain a deep block at a level of <10 post-tetanic counts recorded every 6 min. At recovery of T_2, following at least 2 h of neuromuscular block, patients received their randomly assigned dose of 0.5, 1.0, 2.0, 4.0 or 6.0 mg/ kg of sugammadex. The results showed a dose-related decrease in the average time taken to attain a TOF ratio of 0.9 from 6:49 min with the 0.5 mg/ kg dose to 1:22 with the 4.0 mg/ kg dose.They concluded that sugammadex effectively reversed a deep and prolonged neuromuscular block induced by rocuronium and recommended the effective reversal dose to be 2–4 mg/ kg.Sparr et al[5] evaluated sugammadex for reversal of profound rocuronium-induced neuromuscular blockade in 98 patients, randomized to receive sugammadex (1, 2, 4, 6, or 8 mg/ kg) or placebo at 3, 5, or 15 min after 0.6 mg/kg rocuronium. They found that the mean time to recovery of the TOF ratio to 0.9 after dosing at 3, 5, and 15 min decreased from 52.1, 51.7, and 35.6 min, respectively, after administration of placebo to 1.8, 1.5, and 1.4 min, respectively, after 8 mg/kg sugammadex. The median cumulative excretion of rocuronium in the urine over 24 h was 26% in the placebo group and increased to 58–74% after 4–8 mg/kg sugammadex. The mean plasma clearances of sugammadex and rocuronium were 0.084 and 0.26 l/min, respectively. They concluded that sugammadex safely reversed profound neuromuscular blockade induced by 0.6 mg/kg rocuronium in a dose-dependent manner. Sugammadex enhanced the renal excretion of rocuronium, and its clearance is approximately one third that of rocuronium.Hunter et al[13] mentioned that aminosteroid agents other than rocuronium do not interact as tightly with sugammadex, but animal and human studies suggest that if larger doses of the cyclodextrin (at least 4 mg/kg) are given when T_2 has reappeared, vecuronium can be adequately antagonized. At this early stage, it does seem that sugammadex would need to be given in even larger doses to be efficacious in reversing pancuronium[13]. In contrast, and importantly, sugammadex does not antagonize residual block induced by the benzylisoquinolinium relaxants such as atracurium and mivacurium because of more bulky benzylisoquinolinium structures[13].

Dose-The dose-dependency can be readily explained by the need to bind more rocuronium in plasma as blockade becomes deeper. Thus, even after the introduction of sugammadex, neuromuscular monitoring will be useful, allowing the right dose to be chosen. The alternative would be to give a large sugammadex dose for all cases, a more expensive course of action than monitoring[9]. The other question that needs to be answered relates to the possibility of re-paralysis. If the dose of sugam-madex given is just enough to capture most of the rocuronium in plasma, then there will be sufficient movement of rocuronium away from the neuromus-cular junction down the concentration gradient of free drug into plasma. This may

produce full return of neuromuscular function. However, with time, more rocuronium molecules will be transferred from peripheral tissue into plasma, and there will no longer be enough free sugammadex molecules available[9]. The free rocuronium will then have access to the neuro-muscular junction, where blockade can ensue. Another issue which needs to be tested is to administer sugammadex in divided doses: a first injection to achieve immediate recovery, and a second to make sure there is no recurarization[9]. The tendency to adopt a "one dose fits all" approach for both rocuronium and sugammadex is likely to become expensive and contrary to the patient's best interests.

Advantages-Sugammadex could solve the problems of residual paralysis and failed intuba-tion[9]. If rocuronium is given at induction of anesthesia and the airway cannot be secured, prompt restoration of normal neuromuscular function could be achieved with the appropriate dose of sugammadex[9]. If large doses of rocuronium can be given, the surgeons may be presented with better surgical conditions with a more intense neuromuscular block, and reversal can still be accomplished, because sugammadex appears to be more reliable than neostigmine[18]. When sugammadex becomes available, concerns about reversal of blockade at the end of a case will be diminished. Therefore, anesthesiologists may be tempted to give larger doses of rocuronium than they do now with a benefit of better intubating condi-tions, less delay between induction and laryngoscopy, less desaturation, less airway trauma, better surgical conditions, fewer respiratory problems at emergence, less residual paralysis. Moreover, there were minimal effects on heart rate and arterial pressure following sugammadex administration[4]. As the drug does not act via the nicotinic receptors or by influencing the liberation or metabolism of acetylcholinesterase, there are no muscarinic side-effects associated with its use. Such effects are responsible for the side-effects observed with the use of anticholinesterase agents requiring the concomitant use of anticholinergic drugs. The anticholinergic drugs, in particular atropine, may produce undesirable tachycardia and/or arrhythmias. The absence of cardiovascular and other muscarinic effects during the process of reversal will be of great advantage in patients with cardiovascular and respiratory disease[4].

Other uses-Sugammadex has been used for rescue agent in a patient of renal failure who had residual neuromuscular blockade after the use of neostigmine and had acute respiratory distress[19].

Concerns-However, there are some dan-gers. There could be a greater incidence of aware-ness, because total absence of movement may mask insufficient anesthesia and analgesia[9]. Also, the problem of managing the airway after sugammadex has been given, for instance if a repeat procedure needs to be performed, is not settled[9]. Perhaps there will be a role for succinyl-choline after all. Without knowing the depth of the rocuronium-induced neuromuscular blockade, it would be difficult to know the dose of sugammadex needed. Perhaps conventional nerve stimulators would be sufficient to determine the presence or absence of the twitch response, and the appropriate dose of sugammadex could be administered accordingly. Further, the use of rapid-sequence induction with rocuronium can be facilitated by the presence of sugammadex. Nevertheless, studies are needed to address the role of sugammadex as a"rescue" reversal drug in patients with unanticipated difficult airways who received rocuronium.

Adverse effects-Few adverse effects were reported that were considered related to sugammadex. The common were nausea, vomiting[10] and QTc prolongation[5,8,10,13], hypotension[7], increasesd CPK levels[18], abnormal values for microalbumin, *N*-acetyl-glucosaminidase, and/or microglobulin in urine[5]. The other side effects reported includes dry mouth, parosmia, a sensation of a changed temperature[8].

QTc prolongation was attributed to sevoflurane, propofol, morphine used in these studies[10,12,13] but needs further evaluation. The other issue includes signs characteristic of insufficient depth of anesthesia, such as an increase in Bispectral Index, grimacing, moving, sucking on the tube, and coughing[5,7]. Theoretically, the anesthetic state might also be

changed due to capture of fentanyl and/or propofol by sugammadex. This mechanism, however, is unlikely, because the affinity of sugammadex for narcotics and intravenous anesthetics is negligibly small. These effects may also be due to sudden reversal of neuromuscular block after administration of sugammadex combined with a surgical stimulus at a time of insufficient depth of anesthesia[5,7]. The hypotension may have been related to administration of propofol and fentanyl, rather than to sugammadex[7].

Effect on other drugs- Sugammadex is ineffective against succinylcholine and benzylisoquinolinium neuromuscular blockers, such as mivacurium, atracurium, and cisatracurium, because it cannot form inclusion complexes with these drugs. Therefore, if neuromuscular blockade must be re-established after using sugammadex, succinylcholine or one of the benzylisoquinolinium neuromuscular blockers should be considered. Furthermore, steroidal hormones are also bound tightly to specific protein carriers; for example, the sex hormones are bound with very high affinity to globulin. The possible effects of the sugammadex-induced improved solubility of propofol, midazolam, and bupivacaine on the pharmacodynamics/ pharmacokinetics of these compounds have not yet been studied.There are concerns that cyclodextrins could encapsulate other steroidal drugs and indeed endogenous steroids such as glucocorticoids, sex hormones and aldosterone[13].

Status in renal dysfunction- The role of sugammadex in renal compromised patient has not been studied yet. Recovery from the effect of an i.v. bolus dose of any drug occurs by redistribution, not elimination. This is thought to be the reason why the effect of this selective relaxant binding agent in patients with renal dysfunction is unaltered[13]. Much work is still required, however, in this vulnerable patient group.

Pregnancy and drug-No study for safety profile in pregnant and lactating females has been reported till yet.

Conclusion-In view of the potential of sugammadex to reverse even a profound NMB, and its favorable safety profile, this agent may fulfill the criteria of an ideal reversal agent for rocuronium. Continued safety and efficacy for this promising agent will be confirmed in future clinical studies.

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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.

Update on Prebiotics and Probiotics

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Some facts about human intestine and intestinal microflora

- Intestines [mainly small gut] is the body's most important immune function related organ, where 60% of body's immune cells reside. It controls immune response to dietary antigens [food allergies] and microorganisms entering by oral route[rota and poliovirus, salmonella, listeria, toxoplasma etc.].
- Total number of cells in human body is 10^{14} of which only 10% is mammalian and rest 90% is prokaryotic [often called "MICROFLORA ORGAN"]. This implies a close relation between pro and eukaryotes where bacteria exert a fundamental control. Intercommunication relies on an integrated signalling system where commensal and infectious bacteria produce a whole range of molecules [both pro and anti-inflammatory] and homeostasis is maintained by a balance between them. This balance is disrupted by antibiotics, chemotherapy, radiotherapy, infections.
- Number and type of bacteria/gm of contents in different gut segment is as : oesophagus and stomach - < 10^3, mostly helicobacter and lactobacilli; proximal small gut – 10^4 – 10^6, mostly lactobacilli and Enterococcus fecalis; distal small gut – 10^7, mostly lactobacilli, coliforms and bacteroides; colon – 10^{12}, mostly coliforms, lactobacilli, enterococci, anaerobes [clostridium, bacteroides, bifidobacterium] and methanogenic ones. Humans excrete about 8 gm bacteria in stool/day equal to ¼ dry stool weight.
- At the level of species and strains, every individual harbour its own distinct pattern of bacterial composition [with conseq-uent huge interindividual diversity in this] determined by genetics, environment [including in utero environ-ment with its vertical transmission], diet and disease. In healthy adults, fecal composition is stable over time. The pattern is disrupted in the immunocompromised, debilitated, elderly people and in ICU setting.
- Upper GI tract bacteria have important influences on immune function [acting through Peyer's patches in small gut]. Normal colonic flora maintain integrity of enterocyte, modulate metabolic and immunologic processes and prevent colonisation by invasive microorganisms.
- Human colon is unable to nourish itself from blood, nutrition is derived from luminal contents. These include short chain fatty acid, polyamines, growth factors, amino acids like glutamine, arginine and cysteine [immunonutrients], vitamins and antioxidants which are produced by commensal probiotic protective flora from luminal substrates [called prebiotics]. It is emphasized that 10% calorie and 20% food should be colonic food.
- Probiotic flora is deficient in industrialised nations but adequate in vegans, Asia and Africa.

Definitions

- **Probiotic** – Living microorganism which upon ingestion in adequate number confer health benefits beyond general nutrition [preventive or therapeutic]. The term was coined in 1965 by Lilley and Stillwell.
- **Prebiotic** – Non digestible substances that provide beneficial physiological effect on host by selectively stimulating growth or activity of a limited number [select group] of indigenous favourable bacteria [commensals].

These include non starch oligo or polysaccharides [including fibres, **oligofructose**, inulin, galacto-oligosaccharides, lactulose, breast milk oligosaccharides], complex proteins, shredded mucosal cells, mucin and other GI secretions, some bacterias and yeasts. Oligofructose is naturally found in wheat,onion, banana, honey, garlic, leeks, chicory root. Most prebiotics are used as food ingredients e.g. in biscuits, cereals,chocolate, dairy products. An important characteristic of prebiotic is that no small intestinal enzyme can digest them.

- **Synbiotic** – Combination of pre and probiotic [e.g. baby food]

Function and mechanism of action of probiotics

- Produce essential colonic food from prebiotics.
- Prevent overgrowth of pathogenic microorganisms by - competing for food and adhesion with them and their toxins; producing bacteriocins; pH and redox changes by H_2O_2 production; decreasing their procarcinogenic enzyme production.This stabilise the commensal microflora thus increasing resistance.
- Regulation of intestinal function by-increasing mucin secretion, motility and barrier function by increasing cell survival and their proliferation and differentiation thus decreasing exposure to food antigens; bettering nutrient absorption; scavenging free radicals; improving splanchnic blood flow ; lowering ammonia production.
- Improves bioavailability of nutrients e.g. milk protein, Ca,Mg,Fe along with production of vitamins, folic acid and digestive enzymes.
- Modulates intestinal mucosal immunity by- strengthening innate immunity and modulation of pathogen induced inflammation via toll like receptors which regulates cell signalling pathways like AKt, MAPK and NFKBeta. This lowers exposure of immune cells to toxins and increase protective immunity; activate local macrophages to increase IgA secretion and antigen presentation to B lymphocytes and Peyer's patches, modulate cytokine profile and induce hyporesponsiveness to food antigens; eliminating toxins and unwanted substances e.g. steroid, cholesterol from gut flora.

Effect of antibiotic use on GI function-From above discussion, it is clear that indiscriminate antibiotic use can alter the GI tract microbial ecosystem and normal bacteria – host interaction with disasterous consequences.

- Decreased gut resistance lead to epithelial break, lower absorption and metabolism of nutrients and drugs and increase bacterial invasion. Examples include malabsorption produced by neomycin, decreased enterohepatic circulation of estrogens by ampicillin and vitamin K malabsorption produced by Beta lactam antibiotics.
- Altered susceptibility to infection e.g. salmonella carrier from acute infection or sepsis in carriers,
- Colonisation of body by resistant organisms [in ascending order of resistance colon, perineum, urethra, skin, upper respiratory tract] which contaminate the immediate environment leading to spread of infection e.g to healthy adults living with patient like hospital staff or other patient via hand of personnel.
- Glossitis, gastritis, pruritus and antibiotic induced diarrhoea and colitis.

Formulation-Probiotics are used as food or diet supplement and also as pharmaceuticals and nutraceuticals as tablets, capsule and sachets [freeze dried]. Most common probiotics [functional food] are dairy and dairy products where lactobacilli by fermentation

- Maintain viability, stability and preserve key nutrients, vitamins and antioxidants in storage and even during freeze drying [e.g. increased shelf life in yogurt]
- Produce mild acidity in storage and impart flavour and aroma,
- Eradicate pathogens. Also used in vegetables, animal protein, legume etc.

Types [genus – species – strain]

- Lactic Acid bacteria [include lactobacillus and lactococcus spp., streptococcus thermophilus] – mostly lactobacilli are used e.g. L.plantarum 299V, acidophilus [LA-5, NCFM], casei [DN114 001,CRL431, F19, Shirota], rhamnosus [LGG, LB21], johnsonii La1, reuteri ATTC55730, salivarius UCC118, lactis L1A, bulgaricus.
- Bifidobacterium – longum BB536, lactis [DR10, Bb12], animalis DN 173010, breve Yakult, infantis 35624.
- E.coli Nissle 1917.
- Saccharomyces cerevesiae [boulardii] lyo.
- Enterococcus LAB SF 68
- Mixture e.g. Enterogermina [4 strains of Bacillus clausii like O/C,NR,SIN,T], VSL#3 [1 strain of Strept-ococcus thermophilus, 4 Lactobacillus spp and 3 Bifidobacterium spp strains]

Clinical application

- Diarrhoea-Treatment of acute diarrhoea in children where it reduces severity and duration though mostly in viral ones e.g. L.reuteri, rhamnosus, casei and S.boulardii. Evidence for preventive effect is only suggestive; Treatment of antibiotic associated diarrhoea in children and adults [L.rhamnosus GG, S.boulardii] and prevention and treatment of C.difficile colitis in adults [L.casei, S.boulardii];Treatment of radiation induced diarrhoea [VSL#3] (evidence inadequate).
- Allergy – atopic dermatitis and eczema, food allergy. (evidence inadequate).
- Eradication of H.pylori – both by adjuvant effect and increasing compliance by lowering side effects [enterogermina,lactobacilli spp]
- Hepatic encephalopathy – Lactulose.
- Irritable bowel syndrome – alleviates symptoms [L.rhamnosus, B.infantis, VSL#3].
- Inflammatory bowel disease – maintains remission of ulcerative colitis [E.coli Nissle 1917] and prevent initial attack and maintain remission in pouchitis [VSL#3].
- Lactose malabsorption – some lactobacillus spp reduce symptoms.
- Boosting immune response - decrease post operative infection in ICU, prevent influenza in winter (evidence inadequate).
- Prevention of -cardiovascular disease [by lowering cholesterol], - colon cancer [SYNCAN study], NAFLD (evidence inadequate).
- Necrotising enterocolitis [Bifidobacterium spp] – risk reduced in preterm infants.

Regulation

- Documentation of health effect should be on the specific strain being sold [so listing has to be as genus-species-strain on the sample].
- Results of one strain cannot be held as evidence for efficacy of another untested strain.
- Specific dose [i.e. number of viable cells that will remain till end of shelf life] at which benefit occur has to be mentioned, effect at lower dose cannot be held to produce beneficial effect e.g. in IBS, dose needed for alleviating symptoms was 100 million cfu/day for Bifidobacterium but 300 – 450 billion cfu tid for VSL#3.
- The filler or vehicle has to be mentioned, another cannot be used lest it affect shelf life and storage conditions.
- Viability[i.e. shelf life] has to be mentioned.
- Must be shown to be effective in controlled human studies.
- Safety to be established even by post marketing surveillance.

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Original Article

Cohabitational Effect of Blood Pressure Among Non-Genetically Related Pairs In India

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People who live together come to resemble each other to a greater or lesser degree. This effect is called "cohabitational effect"; the resemblances come through the processes of living together. Cohabitation, or the sharing of the same or similar household environment, usually implies the sharing of many aspects of life style[1]. Thus, individuals who cohabit should show concordance in cardiovascular risk factors that have association with life style, and such concordance should increase with duration of cohabitation. Married couples are pairs who are genetically non-related, but share the environment for a considerable period of time.Spouse concordance is a state where husband and wife are found to have closely similar attributes[2]. Not only do spouses' analysis assist in teasing out the relative contribution of genetic and environmental factors, but such studies might also provide a rationale both for case finding and for environmental modification.As compared to American samples, relatively little is known about marital aggregation of blood pressure in non-western countries in which alternative life styles may affect the expression of traits differently. Another feature that distinguishes western societies from many Indian groups is the homogeneity among family members for many environmental covariates relating to blood pressure.This study is an attempt to find out proportion of concordance of blood pressure among married couples and to study concordance of factors, which affect blood pressure concordance.

Material & methods-this cross-sectional, community based study was conducted from may 2004 to april 2005, in jaripatka, which is an urban area under nagpur municipal corporation. This area was selected for feasibility. The ethics committee of indira gandhi government medical college approved the study. Study subjects were married couples in whom both husband and wife were of the age 30 years or more. Couples in whom the wife was pregnant, and those in whom either or both spouses had secondary hypertension were excluded.initially a pilot study was conducted to test the proforma and to have a rough estimate of the proportion of concordance of blood pressure. The proportion of concordance was found to be 64% in the pilot study. Expecting 20% non-participation, sample size came out to be 260 couples. A house-to-house survey was carried out. It was decided to start with the first house and cover all the houses till the required sample was reached. Informed written consent was obtained from the head of the household and the study subjects after explaining them the objectives of the study.detailed history regarding socio-demographic characteristics was recorded in predesigned, pretested proforma. Dietary history was taken by 24 hour recall method. Visible fat intake per day was then estimated as per icmr guidelines[3]. Level of salt consumption was assessed by simple patient estimation of low (seldom or never) moderate (if needed after tasting) or high (routinely before tasting) salt addition during meals[4]. Current habits regarding physical activity (occupational and leisure-time) were assessed and graded as light moderate and heavy[5]. Stress was assessed by a self-administered questionnaire[6], which was to be filled separately by both spouses. Anthropometric indices including height, weight, waist circumference and hip circumference were measured according to recommended techniques[7]. Body mass index (bmi) and waist-hip ratio (whr) were calculated. A bmi value of 25 to 30 was defined as overweight, and a

value 30 and over, as obese[8]. The criteria for truncal obesity was whr >0.92 for husbands and whr >0.85 for wives[8].fasting blood sugar estimation was done early in the morning after overnight fast, using sure step-plus blood glucose meter (life scan). Subject was considered diabetic if he/she was a known case of diabetes mellitus or if his/her fasting blood sugar was 120 mg/dl or more[9]. Along with blood sugar estimation, blood pressure was also measured in the morning; this ensured that there was no vigorous physical activity, or consumption of hot beverages like tea and coffee, thirty minutes prior to blood pressure measurement. Blood pressure was measured using mercury sphygmomanometer, in the right arm, with subject in sitting position. Two readings were taken over a period of three minutes; both were recorded and mean value considered for analysis. The criteria for considering a subject as hypertensive was : systolic blood pressure ³ 140 mmhg or diastolic blood pressure ³ 90 mmhg or the use of anti-hypertensive medications[10].

Criteria for concordance of various factors

- Blood pressure- Both spouses hypertensive or both normotensive
- Education - Both spouses having same level of education i.e. <12, 12-15, >15
- Type of die- Both spouses consuming same diet, either vegetarian or mixed diet
- Visible for consumption- Both spouses having similar fat intake i.e. <20 or ³20 gm/ day.
- Salt consumption- Both spouses having similar level of salt consumption, either 'low' or 'moderate to high'.
- Physical activity- Both spouses having same level of physical activity i.e. 'light' or 'moderate to heavy' physical activity.
- Body Mass Index- Both spouses at same BMI level i.e.<25, 25-30, ³30.
- Truncal obesity- Presence or absence of truncal obesity in both spouses.
- Stress- Both spouses having same number of life time events, i.e. <10 or ³ 10.
- Diabetes Mellitus- Both spouses diabetic, or both non-diabetic.

Percentage, mean and standard deviation were calculated. Association was tested by applying Chi-square test. Peasrsons correlation coefficient was calculated.

Results and discussion-a total of 287 families were visited in the survey of which 25 were not willing to participate, 14 were not eligible and 10 were not available. The required sample size of 260 couples were obtained in 238 families. All the couples were of hindu religion. 75% husbands were businessman, mostly shop owners; 80% wives were housewife.64.6% couples were married for 10-30 years duration. The minimum and maximum duration of marriage was found to be 6 months and 57 years respectively. As expected, mean age of husbands was more as compared to that of wives (table i). Similar distribution have been reported by speers ma et al (1989)[11] and knuiman mw et al (1996)[1].systolic and diastolic blood pressures were lower for wives than for husbands in the lower age groups. This difference appears to be the general sex difference rather than one between husbands and wives. Systolic blood pressure for husbands and wives increased with age. Diastolic blood pressure increased with age up to 40 years of marriage, after which it lowered both in husbands and wives (table ii). These findings are similar to that of speers ma et al (1986)[12].149 (57.3%) couples were concordant for blood pressure i.e. Both spouses having same level of blood pressure (both normotensive plus both hypertensive) (table iii). Gearing fr et al (1962)[13] found equal number of couples who were concordant and discordant for blood pressure. High concordance was seen upto 20 years of marriage and after 30 years of marriage. The association between duration of marriage and concordance of blood pressure was found to be significant (table iv).concordance of various factors ranged from 43.8% (for bmi) to as high as 87.3% (for visible fat consumption). Concordance for dietary factors was very high among couples. Concordance of all these factors (except diabetes

mellitus) did not explain concordance of blood pressure among couples (table v). When 172 couples in whom both husband and wife were of the age 30 years or more, and those who were not under anti-hypertensive medication were analysed for correlation of blood pressure, correlation coefficient for systolic blood pressure was found to be 0.03 (non significant) and that for diastolic blood pressure was 0.07 (non significant). Correlation coefficient in different marriage duration groups was also non significant. (table vi)higher concordance in the initial period after marriage could be due to high degree of assortative mating among couples. Higher concordance during later years after marriage suggests role of some other unknown shared marital environmental factors which could affect blood pressure concordance among couples. Concordance of blood pressure could not be explained by concordance of various factors like education, dietary factors, physical activity, body mass index, truncal obesity and lifetime stress, among couples. The observed blood pressure concordance was influenced by the concordance of diabetes mellitus among couples. Thus lifestyle interventions that specifically target the marital partners as a unit may be more efficacious than individual patient education strategies, for prevention and control of co-morbid conditions-hypertension and diabetes. Further research on concordance of blood pressure among couples should be done to explain new variables, those that might illuminate the unidentified shared environmental factors that account for the concordance.

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Table-I, Mean age of husbands and wives according to duration of marriage			
Duration of Marriage (Years)	No. of Couples (%)	Mean age (SD)	
		Husbands	Wives
< 10	21 (8.1)	36.0 (3.7)	32.1 (2.7)
10 - 20	77 (29.6)	41.6 (6.1)	36.9 (4.3)
20 - 30	91 (35.0)	49.8 (4.8)	43.7 (4.3)
30 - 40	49 (18.8)	57.8 (4.4)	51.3 (3.8)
³ 40	22 (8.5)	67.8 (5.2)	61.6 (4.5)
Total	260 (100.0)	49.3 (10.0)	43.7 (8.9)

Table-II, Mean Blood Pressure (Systolic and Diastolic) among husbands and wives according to duration of marriage					
Duration of marriage (years)	Total (n=260)	Systolic Blood Pressure (Mean + SD)		Diastolic Blood Pressure (Mean + SD)	
		Husband	Wife	Husband	Wife
< 10	21	127 + 14.7	122.6+10.2	85.4+12.2	80.5 + 8.0
10 – 20	77	129 + 17.7	124.2+13.6	87.1+10.0	82.0+12.5
20 – 30	91	133 + 20.3	130.1+16.1	87.8+11.5	85.1 + 9.3
30 – 40	49	139 + 20.2	142.6 + 17.5	88.0+10.9	90.2 + 9.9
³ 40	22	138 + 22.7	153.3 + 20.7	82.2+12.7	87.3+10.1

Table-III,Distribution of couples according to hypertension	
Hypertension	No. (%)
Both normotensive	84 (32.3)
Both hypertensive	65 (25.0)
Only husband hypertensive	70 (27.0)
Only wife hypertensive	41 (15.7)
Total	260 (100.0)

Table-IV, Duration of marriage and concordance of blood pressure			
Duration of Marriage (years)	Concordance of Blood Pressure		Total
	Present	Absent	
<10	16 (76.2)	5 (23.8)	21 (8.1)
10 – 20	48 (62.3)	29 (37.7)	77(29.6)
20 – 30	41 (45.0)	50 (55.0)	91(35.0)
30 – 40	28 (57.1)	21 (42.9)	49(18.8)
³ 40	16 (72.7)	6 (27.3)	22(8.5)
Total	149 (57.3)	111 (42.7)	260(100)

÷² = 10.07, df = 3, p < 0.05 (Duration of marriage <10, 10-20, 20-30 and e"30 were compared).

Table-V, Concordance of factors associated with Blood Pressure concordance among couples			
Factors	Concordance (n=260)	Concordance of Blood Pressure	c^2, df, P value
Education	151 (58.0)	87 (57.6)	0.01, 1, >0.05
Type of diet	201 (77.3)	112 (55.7)	0.9, 1, >0.05
Visible Fat consumption	227 (87.3)	129 (60.4)	0.17, 1, >0.05
Salt consumption	211 (81.1)	122 (57.8)	0.12, 1, >0.05
Physical Activity	199(76.5)	116(58.3)	0.34, 1, >0.05
Body-mass index	114 (43.8)	63 (55.3)	0.35, 1, >0.05
Truncal Obesity	140 (53.9)	81 (57.9)	0.04, 1, >0.05
Lifetime Stress Events	214 (82.3)	127 (59.3)	2.05, 1, >0.05
Diabetes Mellitus	141 (54.7)	96 (68.1)	14.6, 1, <0.01

**Figures in parentheses indicate percentage.*

Table-VI,Correlation coefficient of blood pressure among couples			
Duration of marriage (years)	No. of Couples	Coefficient correlation (r)	
		Systolic BP	Diastolic BP
< 10	20	-0.01	0.07
10 – 20	65	0.04	0.17
20 – 30	64	-0.04	-0.04
³ 30	23	-0.04	-0.02
Overall	172	0.03	0.07

P>0.05 for all values of r

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