Message from the new editor

Dr. L. Deban Singh,
Editor, JMS.

Dear Members,

I, on behalf of the Journal of Medical Society (JMS), RIMS, Imphal wish you all a “Happy and Prosperous New Year 2008”.

First of all, I express my heartfelt thanks to all of you for giving me the responsibility as the editor for our esteemed journal.

The journal has earned credibility amongst all the readers and institution during a short period of time. It is my great pleasure to lead our journal as a first editor by an anesthesiologist. I will sincerely try my level best to make it as one of the reputed journals in the country.

Besides having a few publications and paper presentation in various journals, conferences and my long association with the JMS and whole hearted willingness to serve as Editor of JMS, it will be a great opportunity for me to guide the journal as a part of continuing research in various specialities of medical sciences.

It is my intension that all manuscripts will also be subjected to peer reviewer who is an expert in the field. The identity of the author and institution will also be concealed so that the reviewer has no bias on the paper concerned. Once more, I request all the authors to follow strictly the “Instructions to authors” inserted in every January issue.

The first issue under my Editorship as 22nd volume of the journal is coming up in the month of January 2008. I believe that the members of the society, authors, peer reviewers, editorial board members and advertisers will continue to help the editor with constructive advice to uplift the journal.

My thanks are due to outgoing editorial team led by Dr. Y. Indibor Singh who has worked so hard for the past 2 years.

Once again, I agree that I will work upto your expectations with honesty and transparency.
Seroprevalence of TORCH in women with still birth in RIMS hospital


Abstract

Objective: To detect infections with Toxoplasma, Rubella, CMV, HSV (TORCH) among women with still birth by demonstrating IgM & IgG antibodies against TORCH complex.

Methods: 43 women with still birth were screened for IgM and IgG antibodies by using ELISA test (Equipar Diagnostica, Italy).

Results: IgM antibodies for Toxoplasma, Rubella, CMV & HSV were found in 4 (9.3%), 3 (6.9%), 10 (23.26%) and 9 (20.93%) of the cases respectively indicating primary infection/relapse (CMV, HSV) during pregnancy. IgG antibodies for Toxoplasma, Rubella, CMV & HSV were found in 25 (58.14%), 29 (67.44%), 31 (72.09%) and 29 (67.44%) respectively.

Conclusion: Routine antenatal screening for TORCH antibodies for women with bad obstetric for early diagnosis and proper management is suggested.

Key words: TORCH, Rubella, CMV, HSV, Toxoplasma, Still birth.

Introduction

Fetal demise is a traumatic experience for both the parents and the obstetrician. Despite the advances in the field of perinatal medicine, significant number of stillbirths continue to occur. Primary infection with Toxoplasma gondii, Rubella, Cytomegalovirus and Herpes simplex virus (TORCH complex) during pregnancy at various stages can lead to congenital infections with unfavourable fetal outcome in the form of spontaneous abortions, intra uterine death, intra uterine growth retardation, still birth, early neonatal death and congenital malformations. Unfortunately the maternal infections are initially asymptomatic or mild so much so that most women are uncertain about whether they have ever had it. Therefore diagnosis of acute TORCH infection in pregnant women is usually established by detection of specific IgM antibodies against TORCH complex. The present study aims at the detection of TORCH infection in women with still birth by detecting IgM and IgG antibodies.

Material and methods

The present study was carried out in the Department of Microbiology, Regional Institute of Medical Sciences (RIMS), Imphal, during January 2002 to September 2003. Serum samples from 43 women with still birth were screened for TORCH IgM and IgG antibodies by using ELISA test (Equipar Diagnostica, Italy) following manufacturer’s instructions. Absorbance reading was taken at 450 nm filter (referencing at 650 nm). The activity index (A1) values of the controls and serum samples were read from the standard curve prepared for each run.

Results

In the present study, the women with still birth were between 20 to 40 years. Table 1 shows the distribution of TORCH antibodies in women.
with still births. Out of 43 women 4 (9.3%) were positive for IgM Toxoplasma antibody, 10 (23.26%) were positive for CMV Ig M antibody, 3 (6.9%) women were positive for Rubella IgM antibody and 9 (20.93%) were positive for HSV IgM antibodies. IgG antibody alone was positive in 25 (58.14%) cases for Toxoplasma, 29 (67.44%) cases for Rubella, 31 (72.09%) cases for CMV and 29 (67.44%) cases for HSV indicating past infection.

Among 26 women who were positive for TORCH IgM antibody mixed infection of all four TORCH was found in 1, Rubella and HSV in 1, Rubella, CMV, HSV in 1 and CMV & HSV in 4.

Most of the women belonged to low socio-economic status (71%) and were illiterate (62%). Congenital malformation was found in 3 cases.

Table 1. Serological analysis for TORCH antibodies in women with still births.

<table>
<thead>
<tr>
<th>Serological analysis</th>
<th>No. of positive</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Toxoplasma Gondii</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM alone</td>
<td>1</td>
<td>9.3</td>
</tr>
<tr>
<td>IgM &amp; IgG</td>
<td>3</td>
<td>58.14</td>
</tr>
<tr>
<td>IgG alone</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>Rubella</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM alone</td>
<td>1</td>
<td>6.98</td>
</tr>
<tr>
<td>IgM &amp; IgG</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>IgG alone</td>
<td>29</td>
<td>67.44</td>
</tr>
<tr>
<td><strong>CMV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM alone</td>
<td>2</td>
<td>23.26</td>
</tr>
<tr>
<td>IgM &amp; IgG</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>IgG alone</td>
<td>31</td>
<td>72.09</td>
</tr>
<tr>
<td><strong>HSV I &amp; II</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM alone</td>
<td>1</td>
<td>20.93</td>
</tr>
<tr>
<td>IgM &amp; IgG</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>IgG alone</td>
<td>29</td>
<td>67.44</td>
</tr>
</tbody>
</table>

Discussion

Primary infection with TORCH complex leads to spontaneous abortions in about 20% of pregnant women and about 80% of these occur within 2 to 3 months of gestation. The prevalence of Toxoplasma varies from place to place depending upon the food habits and association with pets like dogs and cats. In our present study Toxoplasma IgM antibody was found in 9.3% of the mothers having still birth which is comparable with the study of Turbadkar D et al1 who reported 10.5% positivity among women with bad obstetric history. Bhatia VN et al3 and Rajendra B et al4 reported the prevalence of antibodies of Toxoplasma in 12% and 14.66% respectively.

The greatest risk of congenital Toxoplasmosis occurs during the first trimester of pregnancy. However it is during the third trimester that the highest level of transmission occurs. This is thought to be related to the much larger size of the uterus. The transmission rate from a maternal infection is about 45%. Of this 60% are subclinical infections, 9% result in death of fetus and 30% have severe damage such as hydrocephalus, intracranial calcification, retinochoroidittis and mental retardation.5

Rubella infection during pregnancy can lead to congenital infections like cardiovascular defects, eye defects, deafness and it may cause preterm delivery and still birth. In India 10 to 20% of women in the reproductive group are susceptible to Rubella.6 In our study 6.9% of women were positive for Rubella IgM antibody suggesting acute infection and 67.4% of women were positive for IgG antibody indicating past infection. In a retrospective study of 7484 blood samples for Rubella antibody over a period of 15 years (1988-2002) at NICD, Delhi, the immunity status among child bearing women was as low as 49% in 1988 and there was steady rise over the period where it was 87% in 2002. However 10 to 15% of women reached childbearing age group without developing immunity.7

Seropositivity rate for CMV Ig M in our study was 23.26% which is much higher than 8.4% of Turbadkar D et al1 in women with bad obstetric history but comparable with 26.7% of another study8. Primary infection with HSV II and I acquired by women during pregnancy accounts for half of the morbidity and mortality among neonates. The other half results from reactivation of old infection.1 Sero positivity rate for HSV IgM among women with stillbirth
was 20.93% which was comparable with 26.7% reported by Naveen Thapliyal et al but much higher than the rate of 3.6% among BOH. Mixed infections were noted in 6 out of 26 women with primary TORCH infection (IgM+ve). One patient had all 4 TORCH IgM antibodies, one with Rubella and HSV, one with HSV, Rubella and CMV and two with CMV and HSV. Similar observation of mixed infections has been made by other authors. Mixed infections were noted in 6 out of 26 women with primary TORCH infection (IgM+ve). One patient had all 4 TORCH IgM antibodies, one with Rubella and HSV, one with HSV, Rubella and CMV and two with CMV and HSV. Similar observation of mixed infections has been made by other authors.1,8 Among the 43 women studied for TORCH IgM antibodies it is revealed that many women are still negative for TORCH antibodies indicating that there is chance of primary infection with TORCH in further pregnancies and thereby chance of fetal morbidity and mortality cannot be ruled out.

Conclusion
In order to prevent these morbidity and mortality, routine screening for TORCH complex for antenatal cases with bad obstetric history should be carried out for early diagnosis and appropriate management.

References
Study of empyema thoracis in RIMS hospital

Th. Chito Singh, Ksh. Kala Singh, M. Birkumar Sharma, Th. Sudhir Chandra

Abstract
Objective: Empyema thoracis remains a common thoracic problem with challenging management strategies. We reviewed our experience to outline key aspects of the presentation, management and outcome of this condition in our hospital. Methods: We analysed 81 consecutive adult patients, aged 18 to 71 years, treated for empyema thoracis over a period of 3 years at Regional Institute of Medical Sciences (RIMS), Hospital, Imphal. Results: Most of the patients had symptoms attributable to their empyema, with dyspnoea on exertion being the most common symptoms (95.1%). Broncho-pulmonary infection was the most common aetiological factor, in which 65.4% had been treated for pulmonary tuberculosis. Therapeutic thoracentesis was performed in six patients, tube thoracostomy in 76 patients and decortication in 52 patients. Decortication was the most successful mode of treatment. Conclusion: Early adequate surgical drainage and full lung expansion are the aim of the treatment in empyema thoracis. Success of the operative procedures depends on the stage of disease.

Key words: Empyema thoracis, chest drainage, decortication, pneumonia.

Introduction
Empyema thoracis represents a continuum of disease ranging from thin pleural fluid microscopically contaminated by organisms to gross purulence with dense deposition of fibrin and scar within the pleural cavity entrapping the lung. Hippocrates in 600 B.C. defined empyema thoracis as a collection of pus in the pleural cavity and advocated open drainage as its treatment. Since then the management of this condition has posed a challenge to the clinicians. Different well established therapeutic modalities - aspiration, lavage, debridement via video assisted thoracoscopic surgery, intrapleural fibrinolytic therapy, decortication, thoracoplasty and open window thoracotomy are to be considered in the light of the triphasic nature of the disease. These procedures have all been used with varying success rates ranging from 10% to 90%. The success of the procedure involved depends on the stage of the disease at presentation, age of the patient, associated comorbidity and general condition of the patient. No single-stage procedure is suitable for treatment of thoracic empyema.

We reviewed our experience in empyema thoracis with special attention to the clinical profile, procedure used and success rate of each procedure.

Material and methods
Eighty one patients of empyema thoracis treated in RIMS Hospital, Imphal were studied over a period of three years (Jan 2004 to Dec 2006). All the patients were between the age...
group of 18 to 73 years. 58 patients were male and 23 female.

Empyema thoracis was confirmed in all the patients by (1) pleural fluid culture or Gram's stain showing organisms, or (2) documentation of grossly purulent fluid at thoracentesis or thoracostomy. Empyema thoracis resulting from oesophageal operation or perforation were excluded.

Multiloculated empyema thoracis was defined by the presence of two or more collections of pleural fluid observed on chest X-ray, ultrasonography and/or CT scan. Successful procedures were defined by empyema resolution with complete re-expansion of trapped lung and no further surgical intervention was required.

Treatment included multiple therapeutic thoracocentasis, closed tube drainage or decortication. Selection of appropriate treatment was dependent on the duration and extent of disease, age and fitness of the patient. Closed tube thoracostomy was carried out with a chest tube connected to underwater seal drainage bag. Suction was not applied. Chest tube was removed when the daily chest drain output was below 50 ml and improvement in the chest radiograph was noted. Decortication was performed in the organization phase of the empyema thoracis, post-traumatic empyema thoracis, multiloculated or failure to resolve after tube thoracostomy. This operation was carried out through a standard posterolateral thoracotomy with or without rib resection.

Results
Eighty one patients were included in this present study comprising 58 males and 23 females within the age group of 18 to 73 years.

Most of the patients had symptoms attributable to their empyema, with dyspnoea on exertion being the most common symptoms (95.1%), followed by fever (84.0%). Presenting symptoms of the patients is shown in Fig.1.

The aetio-pathogenesis of the patients in the present study is shown in table 1. Sixty nine patients (85.2%) had broncho-pulmonary infection, of which 53 patients had been treated for pulmonary tuberculosis. The antitubercular therapy was started by primary physician before being referred to us. 9 patients had history of firearm injury in the chest and 2 patients had history of stab injury in the chest. One patient who had undergone pneumonectomy in a centre outside the state presented to us with post-pneumonectomy empyema thoracis.

Therapeutic thoracentasis was performed in six patients, of which 4 patients had to undergo tube thoracostomy because of inadequate drainage. Altogether 76 patients underwent tube thoracostomy as primary procedure in 72 cases, and as secondary procedure in 4 patients who was not benifitted by thoracentasis. Of these 76 patients (93.8%), 52 had to undergo decortication. However, 3 other patients who presented with calcified loculated empyema on chest X-ray had decortication as initial mode of treatment. The procedure employed and their success rate are given in table 2.
Postoperative complications were listed in table 3, which includes air leak, surgical emphysema, wound infection and frozen shoulder. All the complicated cases were managed conservatively and improved with time before sending home except frozen shoulder which was subjected to physiotherapy.

Length of hospital stay varied from 8 days to 46 days. One patient with the air leak after decortication took 39 days to subside.

Discussion
Treatment for thoracic empyema requires appropriate antibiotics, prompt drainage of the infected pleural space and lung re-expansion. However, there is no clear consensus on the best way to obtain these objectives. The variable success rates of the procedures can be attributed, in part, to the stage of the empyema at presentation.

Empyema thoracis may be classified based on the chronicity of the disease process. In the initial exudative stage, pleural fluid is free flowing and usually amenable to multiple thoracentesis or by tube thoracostomy. Progression to the fibrinopurulent stage, which begins after 48 hours, results in the formation of fibrin strands throughout the pleural fluid creating a multiloculated pleural space. At this point, closed drainage with chest tube is unlikely to be successful. Progression to the organizational stage which may occur after as little as 1 to 2 weeks virtually requires decortication because of the extensive pleural peel that restricts lung expansion even if the fluid can be successfully drained.

Since many of the infections that cause empyema are indolent, patients are often treated by physicians after their parapneumonic empyema has already reached the fibrinopurulent or organizational stage. Majority of our patients presented in the later stage of the disease with multiloculation, thick-walled uniloculated empyema or with trapped lung.

Tube thoracostomy is usually the initial treatment of acute empyema thoracis. LeMense GP et al reported a success rate of 70% - 85% with tube thoracostomy, which is only 35.6% in our study. This discrepancy is because of the late presentation of our patients. Although about half of the successful patients in tube thoracostomy had some form of pleural thickening radiographically, the natural history and significance of these findings are not known. However, at least some of the patients showed continued radiographic improvement after removal of tubes in limited follow up.

Bilgin M et al reported that video assisted thoracoscopic evacuation and chest tube drainage in situ reduces the necessity of open decortication. However, this is effective only in the fibrinopurulent phase of the disease. Basic elements of intervention - pleural drainage, different evacuation techniques, decortication, thoracoplasty and open window thoracostomy - are well established technical modalities. Majority of our patients presented in the chronic stage of the disease.

Length of hospital stay for empyema thoracis is long because of multiple procedures and coexistent diseases.

Conclusion
The lack of a single ideal treatment modality reflects the complexity of the diagnosis and

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. of patients (%)</th>
<th>Success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>6 (7.4%)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Tube thoracostomy</td>
<td>76 (93.8%)</td>
<td>27 (35.6%)</td>
</tr>
<tr>
<td>Decortication</td>
<td>52 (64.2%)</td>
<td>50 (96.2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air leak</td>
<td>2</td>
</tr>
<tr>
<td>Surgical emphysema</td>
<td>2</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1</td>
</tr>
<tr>
<td>Frozen shoulder</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2. Procedures employed in the treatment.

Table 3. Postoperative complications after decortication
staging of empyema thoracis. Intrapleural drainage remains to be the initial treatment modality in acute stage of the disease. Organized pleural callus requires formal decortication. Decision-making involves a triad consisting of the aetiology of empyema, general condition of the patient and stage of disease, while considering the triphasic nature of development of thoracic empyema.

References

Beetle dermatitis in Manipur

Th. Nandakishore, Roslin L, Romita B, Kalkambe KA

Abstract
Objective: To study the various clinico-morphological pattern of beetle dermatitis in Manipur and to identify the causative beetle in this region. Methods: 362 cases of suspected beetle dermatitis attending the Skin OPD, Regional Institute of Medical Sciences Hospital, Imphal between the period March 2001 and April 2003 were taken up for the descriptive study. Results: There were 204 males (56.35%) and 158(43.65%) females. Maximum number of patients were in the age group 21-30 years (n= 124; 34.25%). Two hundred twenty nine (63.25%) and 133(36.74%) patients belonged to urban and rural areas respectively. The exposed areas namely the neck (n=140; 38.67%), face (n=135; 37.29%) and arms (n= 50; 13.8%) were commonly affected. In 15 patients (4.14%) there were generalized lesions. Morphology of the lesions varied from the classical linear lesions with necrotic centre and pustules in the periphery to ovoid and irregular patches. Small non-descript lesions were also seen in some cases. Main presenting symptoms included burning sensation, pain, tightness and limitation of movement at the affected site. Constitutional features were also noted in those cases with very necrotic and extensive lesions. Maximum cases (56.35%, n=203) presented on the 2nd or 3rd day. The captured beetle belonged to Coleoptera class, Staphylinid family, Paederus genus and semipurpureous species. Conclusion: Blister dermatitis is a common easily treatable seasonal dermatitis with little symptoms and complications. However a proper diagnosis is essential to allay anxiety among the victims and proper recognition of such common disorders is also necessary for medical personnel to avoid inappropriate treatment.

Key words: Beetle, paederus, dermatitis.

Introduction
Beetle dermatoses have been recognized as a common seasonally occurring dermatitis. Although there are more than 2, 80,000 species, common beetles which are dermatologically relevant belong to two families namely Meloidae (Blister beetle) and Staphylinidae (Rove beetles). They cause either a vesicant (irritant) reaction from powerful irritants contained in their body fluids or allergic contact dermatitis the former being more commoner.

Blister beetles are found in Europe, United states and Africa whereas rove beetles has a worldwide distribution and has been found frequently in tropical areas of the Orient, Africa, South America and Australia. Blister beetles cause acute dermatitis which are not properly recognized or misunderstood though this dermatitis is quite common and known to occur seasonally affecting all populations alike.
Though there are many reports of such dermatitis both in India\textsuperscript{3-8} and abroad\textsuperscript{9-11} no such studies has been undertaken in North-East India including Manipur. This study was conducted to investigate the incidence, extent and clinical patterns of beetle dermatitis and to identify the causative beetle in this region.

**Material and methods**

The study was carried out on 362 patients with suspected beetle dermatitis attending the Skin OPD, Regional Institute of Medical Sciences, Imphal during the period of March 2001-April 2003. A medical history was recorded and clinical examination was performed. Skin biopsies were taken in a few cases. Suspected beetles were caught and species identified in consultation with the Department of Life Sciences, Manipur University.

**Results**

Out of the 362 cases included in the study, there were 204 males (56.35\%) and 158\% (43.65\%) females. The youngest patient was 1-1/2 yr and the oldest 68 yr. Most of the cases belonged to the age group of 21-30 years comprising of contact with any insects. Table 2 shows the site of lesions affected in patients with Paederus dermatitis. The exposed areas of face, neck and arms were commonly affected. The most common site was the neck seen in 140 (38.67\%) patients and 135 (37.29\%) patients had lesions on the face. Involvement of the scalp was rare, seen in only 6 patients (1.65\%). Fifteen (4.14\%) patients had generalized lesions involving more than 3 sites (face, trunk, and upper thighs). Involvement of the flexural areas like cubital and popliteal fossa showing kissing lesions was also common. Morphology of the lesions varied from the classical linear lesions with necrotic centre and pustules in the periphery (Fig 1) to ovoid and irregular patches. Small non-descript lesions were also seen in some cases. Lymphadenitis was not seen in our cases.

Main presenting symptoms included burning sensation, pain, tightness and limitation of movement at the affected site. Itching was minimal to absent. Constitutional features like fever were also noted in a few cases when the lesions were very necrotic and extensive. Maximum number of patients 203\% (56.35\%) presented on the 2\textsuperscript{nd} or 3\textsuperscript{rd} day. Only 31 (8.5\%) patients were unaware of any direct

<table>
<thead>
<tr>
<th>Sites</th>
<th>Number*</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td>140</td>
<td>38.67</td>
</tr>
<tr>
<td>Face</td>
<td>135</td>
<td>37.29</td>
</tr>
<tr>
<td>Arms</td>
<td>50</td>
<td>13.8</td>
</tr>
<tr>
<td>Chest</td>
<td>10</td>
<td>2.7</td>
</tr>
<tr>
<td>Shoulder</td>
<td>15</td>
<td>4.14</td>
</tr>
<tr>
<td>Axilla</td>
<td>8</td>
<td>2.2</td>
</tr>
<tr>
<td>Scalp</td>
<td>6</td>
<td>1.65</td>
</tr>
<tr>
<td>Generalised</td>
<td>15</td>
<td>4.14</td>
</tr>
</tbody>
</table>

\*The number of lesion sites affected is more than the actual number of patients (n=362) as in many patients more than one site was involved.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Male</th>
<th>Female</th>
<th>Total(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>18</td>
<td>19</td>
<td>37(10%)</td>
</tr>
<tr>
<td>11-20</td>
<td>64</td>
<td>52</td>
<td>116(32%)</td>
</tr>
<tr>
<td>21-30</td>
<td>71</td>
<td>53</td>
<td>124(34%)</td>
</tr>
<tr>
<td>31-40</td>
<td>37</td>
<td>16</td>
<td>53(15%)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>14</td>
<td>18</td>
<td>32(9%)</td>
</tr>
<tr>
<td>Total</td>
<td>204</td>
<td>158</td>
<td>362(100%)</td>
</tr>
</tbody>
</table>

124 (34.25\%) patients (Table 1). Children were least affected. Two hundred twenty-nine (63.25\%) and 133(36.74\%) patients belonged to urban and rural areas respectively. Most of the patients gave history of sleeping in the night with lights on. Two hundred thirty-five (64.4\%) patients noticed the lesions in the morning after waking up while washing the face. However, many of them were unaware of any direct

![Fig 1. Classical Paederus dermatitis lesions on the neck.](image)
Biopsy of the lesions showed mostly necrosis of the epidermis with inflammatory cell infiltration in the early phase (day 2/3) whereas subcorneal pustules with heavy polymorphonuclear cell infiltration in those presenting late (day 4/5) (Fig 2).

Incidence of the disease was very high during hot and wet weather. In the year 2001, there were double peaks in the incidence of the dermatitis during the months of May and September coinciding with heavy rains including flood during these months (Fig 3). In the year 2003 maximum cases occurred during the month of April.

Incidence of the disease was very high during hot and wet weather. In the year 2001, there were double peaks in the incidence of the dermatitis during the months of May and September coinciding with heavy rains including flood during these months (Fig 3). In the year 2003 maximum cases occurred during the month of April.

The captured beetle measured about 3-8mm in length with red thorax, greenish black body, dark brown antenna and was identified as belonging to Coleoptera class, Staphylinid family, Paederus genus and semipurpureous species (Fig 4).

Discussion
Da Silva from Brazil first described Paederus as a cause of dermatitis in 1912, and Lehman et al in 1955 described blister beetle dermatitis. Subsequently many reports came from Sri Lanka, Australia and America and in India reports have come from Punjab, Rajasthan, South India and Eastern India. Different geographical areas may report the incidence at different times of the year. In Manipur rainy season generally occurs during May to September but pre monsoon showers also occurs quite frequently during February to April. Though most Indian studies have recorded beetle dermatitis in the post monsoon period particularly, during April-September, our findings also support the eastern Indian report that in the sub-Himalayan region, incidence of beetle dermatitis occurs perennially as rains occur in protracted period during the year. Humid environment seems to be fertile for the propagation of the beetle as even during rainy season no dermatitis is reported if drought occurs as seen in June –July 2001. Clustering of cases which were noticed at the time of heavy rain and flood seen in May and Sept 2001 and low incidence in cooler months November to February in our study corroborated findings of other studies.

There was no predilection of age, sex, rural or urban in the occurrence of the disease as the dermatitis depended on the patient’s activities and insect habitat.

In our series 235 patients (64.5%) noticed the lesions in the morning further corroborating the nocturnal habit of the insects. As reported in other studies where exposed parts particularly face and neck of the body contributed for most number of lesions when the insects easily come into contact with. However covered parts can also be involved. Other than producing local irritant dermatitis-like picture as reported by other workers, our study also revealed that the dermatitis can become generalized involving face, trunk, covered parts even masquerading as eczema-tous dermatitis. Complications included post inflammatory hyperpigmentation in most of the cases.

Biopsy of the lesions revealed initial toxic effect characterized by necrosis, inflammatory cell infiltration and polymorphonuclear cell infiltration as the lesion progressed.
Paederus beetles are nocturnal and are attracted by incandescent and fluorescent lights and as a result inadvertently come into contact with humans. However, daytime contact may also occur as revealed by significant number of patients affected in outdoor also. Hemolymph of the beetle contains paederine which is released on crushing of the insect onto the skin due to reflex of brushing away the insect. Paederin, an alkaloid is largely produced by adult female beetles. Blister formation is the result of activation or release of neutral serine proteases which act on the desmosomal region resulting in intraepidermal separation with little scarring but significant post inflammatory pigmentation. There are more than 30 species of Paederus which can cause dermatitis. Indian reports have mentioned Paederus melampus as the commonest\textsuperscript{14}, P.fuscipes, P.irritants, P.sabaeus, P.himalayicus being other species identified\textsuperscript{1}. \textit{Paederus semipurpureus} is the species identified in our region. Clinically, paederus dermatitis should be differentiated from herpes simplex, herpes zoster, liquid burns, and acute allergic or irritant contact dermatitis from other causes. Linear appearance of the lesions, their predilection for exposed areas, and the presence of kissing lesions are very characteristic. Histopathological and epidemiological features also help in making definite diagnosis.\textsuperscript{14}

\section*{Conclusion}
Blister dermatitis is not an uncommon seasonal dermatitis with little symptoms but can be a source of apprehension for the patient for more serious conditions which look morphologically similar and is noteworthy for cosmetic consideration. A proper diagnosis and treatment is therefore essential to allay anxiety among the victims which requires awareness of such common disorders amongst the medical personnel.

\section*{Acknowledgement}
The authors wish to express their gratitude to Prof. T. Kameshwar Singh, Dept of Life Sciences, Manipur University for his valuable expertise in the identification of the beetle involved in the present study.

\section*{References}
Effect of Azadirachta indica Linn. aqueous leaf extract on blood glucose in adrenaline induced hyperglycemia in albino rats.

Lakshman Das, Ng. Gunindro, S. Rita, R.K. Bharati

Abstract

Objective: To evaluate the effect of Azadirachta indica aqueous leaf extract (ALE) on blood glucose in normal as well as adrenaline induced hyperglycemic albino rats.

Methods: Effects of ALE (500 and 1000 mg/kg p.o.) on blood glucose levels were evaluated in normal and adrenaline (0.5 mg/kg i.p.) induced hyperglycemic albino rats. Blood glucose levels were measured just prior to and after 30, 60 and 120 min of ALE administration. The control and standard drugs used were 5% gum acacia suspension (5ml/kg p.o.) and glibenclamide (0.5 mg/kg p.o.) in 5% gum acacia suspension respectively.

Results: Blood glucose levels of normal rats, treated with ALE (500 and 1000 mg/kg p.o.) showed significant reduction (p<0.05) as compared to control. The maximum reduction of blood glucose was observed at 60 min. The hyperglycemic response to adrenaline (0.5 mg/kg i.p.) was not reduced by ALE (500 and 1000 mg/kg p.o.) treatment. Conclusion: ALE produces fall in the blood glucose level in normal albino rats. However, ALE fails to reduce adrenaline induced hyperglycemia suggesting that it does not have inhibitory effect on glycogenolysis.

Key words: Azadirachta indica, blood glucose, adrenaline induced hyperglycemia,

Introduction

Diabetes mellitus is a metabolic disorder in which the body does not produce or properly use insulin. It causes disturbances in carbohydrate, protein and lipid metabolism leading to complications such as retinopathy, microangiopathy and nephropathy. Currently available antihyperglycemic agents for clinical use have characteristic profile of side effects.

In accordance with the WHO expert committee on diabetes mellitus, investigation of antihyperglycemic agents of plant origin used in traditional medicine is considered important. Many herbs and plant products have been shown to have antihyperglycemic action. Azadirachta indica Linn. has been mentioned to possess a number of pharmacological effects like hypoglycemic, hypotensive, antiserotonin, anti-inflammatory and hepatoprotective.

The objective of the present study was to evaluate effect of Azadirachta indica Linn. aqueous leaf extract on blood glucose in normal as well as adrenaline induced hyperglycemic albino rats.

Material and methods

Animals: Albino rats of Wistar strain (150 - 200g) of either sex were used. Animals were obtained from the RIMS central animal house and kept in polypropylene cages in the departmental animal house. They were acclimatized for 10 days and fed on standard diet.
laboratory diet with water ad libitum. 12 hours light and dark cycle was maintained.

Laboratory practice:
The Institutional Ethics Committee of RIMS, Imphal approved the protocol of the study.

Preparation of the extract:
Fresh leaves of Azadirachta indica (family - Meliaceae), a tree known as Neem were collected during the month of June and July, and authenticated. The aqueous extract of the leaves was obtained by the procedure as described by Khosla et al.5 One kg of freshly collected, shade dried, powdered leaves of A. indica were ground and soaked in 4 litres of distilled water overnight. The suspension was centrifuged at 5000 rpm for 20 min and filtered through Whatman No.1 filter paper. The supernatent fluid was allowed to evaporate in sterile petridishes. After drying, the extract was collected by scrapping and stored. The yield was 12.5%. The extract was found to be safe up to 2g/kg p.o. in albino mice.

The effect of A. indica aqueous leaf extract was studied both in normal and adrenaline induced hyperglycemic rats.

1. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in normal albino rats.

24 albino rats weighing 150 -200 g were used for the experiment. They were divided into 4 groups of 6 animals in each group and kept fast for 18 h with free access to water. Care was taken to prevent corpophagy. Blood samples were collected from orbital sinus for glucose estimation. Then the animals were treated as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group - I (control)</td>
<td>Aqueous 5% gum acacia (5 ml/kg, p.o.)</td>
</tr>
<tr>
<td>Group - II (test -1)</td>
<td>ALE (500 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
<tr>
<td>Group - III (test - 2)</td>
<td>ALE (1000 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
<tr>
<td>Group - IV (standard)</td>
<td>Glibenclamide (0.5 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
</tbody>
</table>

Test and standard drugs were given using 5% aqueous gum acacia suspension as vehicle. Blood samples were collected from orbital sinus at 30, 60, and 120 min after drug administration. Blood glucose was estimated by glucose oxidase method.6 Results were analysed by One-way ANOVA followed by Dunnett's 't' test. P<0.05 was considered to be statistically significant.

1. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in normal albino rats.

Blood samples were collected for glucose estimation just prior to and at 30, 60 and 120 min after drug administration. The results were analysed by One-way ANOVA followed by Dunnnett's 't' test. P<0.05 was considered to be statistically significant.

Results

1. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in normal albino rats.

ALE at the dose of 500 mg/kg p.o. reduced blood glucose significantly (p<0.01) at 60 min as compared to control. The dose of 1000 mg/kg p.o. of the extract produced significant reduction of blood glucose at 30 min (p<0.01) as compared to control and the hypoglycemia continued to persist significantly (p<0.001) at the 60 and 120 min. The maximum reduction of blood sugar was seen at 60 min. The reduction of blood glucose levels by glibenclamide (0.5 mg/kg p.o) at 60 and 120 min were highly significant (p<0.001) as

1. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in adrenaline induced hyperglycemia.

Effect of A.indica aqueous leaf extract on adrenaline induced hyperglycemia was studied by the method of Gupta et al7 and Anturlikar et al.8 24 Wistar albino rats of either sex weighing 150 - 200g were divided into 4 groups of 6 animals in each group. After 18 h fasting with free access to water, the rats were treated as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group - I (control)</td>
<td>Aqueous 5% gum acacia (5 ml/kg, p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
<tr>
<td>Group - II (test -1)</td>
<td>ALE (500 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
<tr>
<td>Group - III (test - 2)</td>
<td>ALE (1000 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
<tr>
<td>Group - IV (standard)</td>
<td>Glibenclamide (0.5 mg/kg p.o.) + Inj. Adrenaline hydrochloride (0.5 mg/kg i.p.)</td>
</tr>
</tbody>
</table>

Blood samples were collected for glucose estimation just prior to and at 30, 60 and 120 min after drug administration. The results were analysed by One-way ANOVA followed by Dunnnett's 't' test. P<0.05 was considered to be statistically significant.

Results

1. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in adrenaline induced hyperglycemia.

ALE at the dose of 500 mg/kg p.o. reduced blood glucose significantly (p<0.01) at 60 min as compared to control. The dose of 1000 mg/kg p.o. of the extract produced significant reduction of blood glucose at 30 min (p<0.01) as compared to control and the hypoglycemia continued to persist significantly (p<0.001) at the 60 and 120 min. The maximum reduction of blood sugar was seen at 60 min. The reduction of blood glucose levels by glibenclamide (0.5 mg/kg p.o) at 60 and 120 min were highly significant (p<0.001) as
compared to control group (Table 1).

2. Effect of A. indica aqueous leaf extract (ALE) on blood glucose in adrenaline induced hyperglycemia.

The hyperglycemic response after adrenaline (0.5 mg/kg i.p.) was seen maximum at 60 min. ALE at the doses of 500 and 1000 mg/kg p.o. failed to reduce adrenaline induced hyperglycemia, but there was significant increase (p<0.05) in the blood glucose level as compared to control group. The hyperglycemic responses of adrenaline at 60 and 120 min were reduced significantly (p<0.05) by glibenclamide (0.5 mg/kg p.o) (Table 2).

Table 1. Effect of A.indica aqueous leaf extract (ALE) on blood glucose in normal albino rats.

<table>
<thead>
<tr>
<th></th>
<th>Fasting</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>89.5 ± 6.18</td>
<td>88 ± 6</td>
<td>90.5 ± 5.47</td>
<td>91 ± 8.97</td>
</tr>
<tr>
<td>Test - 1</td>
<td>92 ± 5.79</td>
<td>86.5 ± 6.5</td>
<td>80.5 ± 5.89*</td>
<td>84.5 ± 8.02</td>
</tr>
<tr>
<td>Test - 2</td>
<td>90 ± 6.83</td>
<td>75.5 ± 7.58*</td>
<td>64 ± 5.76**</td>
<td>72 ± 8.46**</td>
</tr>
<tr>
<td>Standard</td>
<td>91 ± 5.55</td>
<td>79.5 ± 8.34</td>
<td>69.5 ± 6.69**</td>
<td>68 ± 8.53**</td>
</tr>
</tbody>
</table>

One - way ANOVA F 0.21 4.05 23.33 9.22
p >0.1 <0.025 <0.01 <0.01

Values are mean ± SD; n = 6 in each group, *p <0.01, **p <0.001 as compared to control (Dunnett's 't' test).

Table 2. Effect of A.indica aqueous leaf extract (ALE) on adrenaline induced hyperglycemia.

<table>
<thead>
<tr>
<th></th>
<th>Fasting</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>89 ± 3.32</td>
<td>103.5 ± 6.31</td>
<td>159 ± 6.28</td>
<td>150 ± 6</td>
</tr>
<tr>
<td>Test - 1</td>
<td>91.5 ± 3.06</td>
<td>113.5 ± 4.08</td>
<td>186.5 ± 10.15 *</td>
<td>180 ± 6.35*</td>
</tr>
<tr>
<td>Test - 2</td>
<td>88 ± 4.24</td>
<td>136 ± 6.51</td>
<td>178 ± 5.54*</td>
<td>161 ± 6.98*</td>
</tr>
<tr>
<td>Standard</td>
<td>92 ± 3.89</td>
<td>114.5 ± 11.0</td>
<td>140 ± 6.26*</td>
<td>116 ± 5.54*</td>
</tr>
</tbody>
</table>

One - way ANOVA F 0.725 20.72 48.26 111.01
p >0.05 <0.001 <0.001 <0.001

Values are mean ± SD; n = 6 in each group, *p<0.05 as compared to control (Dunnett'test).

Discussion
In the present study, the two doses of 500 and 1000 mg/kg p.o. of Azadirachta indica aqueous leaf extract (ALE) produce hypoglycemic effect in normal rats. This finding is in agreement with the reports of other workers.5,9 Maximum reduction of blood sugar is observed at 60 min after administration of the extract. ALE at the dose of 1000 mg/kg p.o. produces more hypoglycemic effect as compared to 500 mg/kg dose.

Adrenaline is the most potent stimulant of hepatic glycogenolysis and gives rise to glucose 6-phosphate, which readily enters the circulation and increases the blood glucose level.10 In our study, hyperglycemia is seen at 30, 60 and 120 min after adrenaline administration. Both the doses of 500 and 1000 mg/kg p.o. of ALE fail to reduce this hyperglycemic response as compared to control. This finding is in variance with Murty et al.6 Failure to reduce adrenaline induced hyperglycemia shows that Azadirachta indica aqueous leaf extract is devoid of inhibitory effect on glycogenolysis. The hypoglycemic effect of the extract in normal rats will be due to its effects on other metabolic processes other than inhibition of glycogenolysis.

Conclusion
The present study shows that Azadirachta indica aqueous leaf extract produces fall in
blood glucose level in normal rats. It does not reduce elevated blood glucose level after adrenaline administration. The failure to reduce adrenaline induced hyperglycemia signifies that the extract does not have inhibitory effect on glycogenolysis.

References


Bone marrow metastasis of solid tumours


Abstract

Objective: To study the spectrum of bone marrow metastasis of solid tumours in Regional Institute of Medical Sciences (RIMS) Hospital, Imphal. Methods: Retrospective analyses of 905 bone marrow aspirates conducted during the period from June 2000 to May 2005 in the department of Pathology, RIMS, Imphal, Manipur, was done. Detailed clinical data, investigation results including complete haemogram were collected from the medical record section. Bone marrow smears were re-examined independently by two haematopathologist. Results: Out of the 905 cases analyzed, metastatic infiltration in bone marrow was encountered in 22 cases (2.43%). In 8 cases (36.36%), the primary sites could not be ascertained because of the undifferentiated morphology. Among children, all the 4 cases (18.18%) were Neuroblastoma. In adults, the primary sites were breast (13.63%) and GIT (13.63%). There were 2 cases (9.09%) each from carcinoma prostate and lung. The age group ranged from 10 months to 75 years with mean age of 55 years. Male to female ratio was 1.3:1. Majority of the patients were more than 45 years. Conclusion: Bone marrow examination is an effective, economical and easy procedure in detecting solid tumour metastasis. It may, therefore be considered to be included in the routine investigation panel for cancer patients.

Key words: Bone marrow, metastatic tumours.

Introduction

Bone marrow (BM) is one of the most common sites of tumour metastasis via blood stream and signifies poor prognosis. It is therefore considered imperative to rule out BM involvement in malignancies like neuroblastoma, carcinoma breast, lungs and prostate where curative treatment is envisaged. BM examination has been found to be increasingly useful in documenting metastatic deposits of tumours having predilection for haematogenous spread.

In adults, carcinomas of breast, lung and prostate account for majority of metastasis in bone marrow specimens. Less common sources of malignancies are gastrointestinal tract, kidneys and skin. In children neuroblastoma, rhabdomyosarcoma and Ewing's sarcoma constitute the majority of BM metastasis. BM evaluation is also done for staging of lymphomas and other malignant tumours.

BM infiltration is suspected on the basis of bone pains, pathological fractures, lytic or sclerotic lesions on X-ray, hypercalcaemia, elevated serum alkaline phosphatase or unexplained haematological abnormalities such as

1. Demonstrator; 2. Asst. Professor; 3. Professor, Department of Pathology, Regional Institute of Medical Sciences (RIMS), Imphal-795004 Manipur, India.

Corresponding author:
Dr. Laishram Rajesh Singh, Department of Pathology, RIMS, Lamphelpat, Imphal-795004 India.
Phone: 91-0385-2427280 Fax: 91-385-2400727
E-mail: rajeshlaish@rediffmail.com.
leukoeerythroblastic picture etc. However, metastasis missed by bone scans and radiographic pictures, may be detected in random marrow aspirates.6

We reviewed BM aspirates with metastatic involvement during the last five years and evaluated haematological findings and associated changes in haemopoietic and stromal elements of BM.

Material and methods
The retrospective study was carried out at RIMS Hospital, Imphal, Manipur. Detailed clinical and investigation data were collected from medical record section. A total of 905 bone marrow aspirations was performed during the period June 2000 to May 2005. BM smears collected were re-examined by two haematopathologist independently. Smears were routinely stained by Leishman’s stain. Special stains such as Periodic Acid Schiff’s (PAS) stain, Myeloperoxidase and Iron stains were also used for some selective cases.

Cases subjected to BM examinations were as a part of tumour staging (13 cases) or due to development of severe anaemia (4 cases) or bone pains (2 cases) or for investigating pyrexia of unknown origin (3 cases).

Results
A diagnosis of metastatic infiltration in BM was encountered in 22 cases (2.43%) of which 18 (81.81%) were in adults and 4 (18.18%) in children. The age group ranged from 10 months to 75 years with mean age of 55 years. (Table.1) Male to female ratio was 1.3:1. Most of the patients were more than 45 years. In 8 cases (36.36%), the findings were incidental and primary sites could not be ascertained. Among children, all the 4 cases (18.18%) were metastatic neuroblastomas(Fig 1). In adults, the primary sites were breast (3 cases, 13.63%) (all females) and GIT (3 cases, 13.63%) (1 male and 2 females). There were 2 cases (9.09%) each from carcinoma prostate (Fig 2) and lung (1 male and 1 female) (Table 2).

![Fig 1](image1.png)

![Fig 2](image2.png)

From the records of peripheral blood examination, all the patients were found to be anaemic with hemoglobin ranging from 5.6 to 9.0 g %. Thrombocytopenia was recorded in 11 (50%) cases while leucopenia was present in 2 (9.09%) cases. Leucoerythroblastic picture was documented in 9 (40.9%) cases.

BM smears in 18 cases (81.81%) were hypocellular, 3 cases (13.64%) normocellular and one case (4.55%) was hypercellular. In 4 cases of neuroblastomas, BM aspirations were done as a part of staging. Diagnosis of adeno-carcinomas was made in 8 cases on the basis of glandular pattern, presence of signet ring cell and mucin detected by PAS. In the remaining cases, the cell clusters were undifferentiated malignant cells and it was not possible to identify their tissue of origin from marrow aspirate.

### Table 1. Age distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of cases.(22)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>4</td>
<td>18.18</td>
</tr>
<tr>
<td>11-20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>21-30</td>
<td>1</td>
<td>4.54</td>
</tr>
<tr>
<td>31-40</td>
<td>2</td>
<td>9.09</td>
</tr>
<tr>
<td>41-50</td>
<td>2</td>
<td>9.09</td>
</tr>
<tr>
<td>51-60</td>
<td>5</td>
<td>22.73</td>
</tr>
<tr>
<td>Above 60</td>
<td>8</td>
<td>36.36</td>
</tr>
</tbody>
</table>

### Table 2. Primary sites of bone marrow metastasis

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Primary Sites</th>
<th>No. of Cases (Total = 22)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Neuroblastoma</td>
<td>4</td>
<td>18.18</td>
</tr>
<tr>
<td>2</td>
<td>Breast</td>
<td>3</td>
<td>13.63</td>
</tr>
<tr>
<td>3</td>
<td>GIT</td>
<td>3</td>
<td>13.63</td>
</tr>
<tr>
<td>4</td>
<td>Lungs</td>
<td>2</td>
<td>9.09</td>
</tr>
<tr>
<td>5</td>
<td>Prostate</td>
<td>2</td>
<td>9.09</td>
</tr>
<tr>
<td>6</td>
<td>Others (undifferentiated)</td>
<td>8</td>
<td>36.36</td>
</tr>
</tbody>
</table>
FNAC slides from primary sites were available in 14 cases. In 8 cases primary could not be ascertained as either results of roentgenographic studies were negative or patients were lost to follow-up.

**Discussion**

BM aspirations are now employed in the investigation of many disorders in haematology, oncology and internal medicine. Detection of metastatic tumours in BM is of great importance for the clinical staging of tumour spread because it influences the response to treatment and the overall survival. Patients with metastatic tumour cells in BM usually have a normochromic, normocytic anaemia and less commonly, thrombocytopenia or neutropenia. In less than half the patients with bone marrow metastasis, the blood films contain some erythroblast and neutrophil precursors (leukoerythroblastic anaemia). In our study, leucoerythroblastic picture was seen in 40.9% cases similar to the study conducted by Sharma S et al where the leucoerythroblastic picture was seen in 50% cases. In adults, the tumors that most commonly metastasize to marrow are carcinomas of prostate, breast, lung, thyroid and kidney. In children they are neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma and retinoblastoma.

In a study conducted by Sharma S et al, neuroblastoma (12%) and breast tumours (12%) predominated. These results are comparable to our study where neuroblastoma (18.18%) predominated among all the metastatic solid tumours in BM, followed by breast and gastrointestinal tract tumours (13.63%) each. Mohanty SK et al in their study of 73 cases reported neuroblastoma in 27 (36.98%) cases followed by 22 (30.13%) cases of carcinoma prostate and 13 (17.81%) cases of breast cancer. In our study, carcinoma prostate was found in 2 cases (9.09%).

Often, it is not possible to identify the primary tumour on the basis of the morphologic features of metastatic cells in marrow smears. Information on the nature of malignant cells may be obtained by immunocytochemistry and immunohistochemistry which are available in selected centres only.

**Conclusion**

BM aspiration is an important part of routine investigation of cancer patients. It may identify metastasis where radiography and bone scans have failed. It is effective, practical and economical in detecting solid tumours metastasis to BM in selected group of patients and rightly considered mandatory for staging of solid malignant tumours.

**References**

Anaesthesia in laparoscopic surgery

L. Deban Singh, GS Moirangthem

Laparoscopy is a surgical technique whereby organs, vessels and other structures of the abdomen and pelvis are visualized and dissected by developing a small video camera and surgical instruments through trocars inserted through small skin incisions in the abdominal wall.

Gynecologists pioneered its widespread use for surgery of pelvic organs in the 1970s. Most recently, general surgeons have taken laparoscopy for many surgeries (about 11% of all operations). The first laparoscopic cholecystectomy (LC) was performed by Phillipe Mauret in France in 1987.

Anaesthesiologists caring for patients undergoing laparoscopic surgeries should be knowledgeable of the specific benefit of laparoscopy, recognized the unique physiologic changes caused by insufflation and anticipate the special hazards (e.g. visceral injuries, blood loss, capnothorax) associated with this surgical technique.

Physiologic changes: The important physiological changes in several organ systems during laparoscopic surgery are brought about by patient position, insufflating gas and body's response to increased intra-abdominal pressure (IAP) following pneumoperitoneum for successful performance of the surgery.

Patient position

The changes associated with positioning may be influenced by the extent of the tilt, patient's age, intravascular volume status, associated disease, anesthetic drugs administered and ventilation techniques. Patients are usually positioned in head down or head up positions.

a) Head down position (Trendelenburg, 100-200)

This position is commonly requested during insertion of Verees needle and trocar insertion and in lower abdominal surgery e.g. gynecologic and GIT surgery like abdominal hysterectomy, appendicectomy and herniorhaphy.

i) Haemodynamic changes: There is an increase in venous return (VR), right atrial pressure (RAP), central blood volume and cardiac output (CO). In contrast, other reports indicate that MAP and CO usually remains unchanged or decrease, although the Trendelenburg position increases preload. These seemingly paradoxical responses may be explained by carotid and aortic baroreceptor-mediated reflexes. CVP increases by an average 8 mmHg at IAP of 15 mmHg in the supine position. It increases by an additional 6mmHg at similar IAP in the Trendelenburg position.

ii) Respiratory changes: Head down tilt causes a cephalad shift in abdominal viscera and diaphragm. Functional residual capacity (FRC),
total lung volume (TLV), pulmonary compliance, VC and diaphragmatic excursion are decreased thus predisposing to atelectasis. There is an increase in the likelihood of hypoxaemia in patients with obese and pre-existing lung disease.

Right mainstem bronchus intubation with inadvertent single-lung ventilation and its associated complications like hypercarbia, hypoxemia and bronchial constriction are possible. There is a tendency for the trachea to shift upward so that a tracheal tube anchored at the mouth may migrate into the right mainstem bronchus and hypoxemia due to cephalad displacement of the diaphragm and carina during insufflation of the abdomen.

iii) Other changes: Nerve compression, brachial plexus injury and elevation of ICP and IOP have been reported.

b) Head up tilt (Reversed Trendelenburg, rT, 20°-30°)

For upper abdominal surgeries, after insufflation the patient's position is usually changed to a steep head up position to allow the viscera to settle down by gravity away from the operative site and facilitate surgical dissection.

i) Haemodynamic changes: The prolonged head up position in upper abdominal surgeries results in decrease in venous return (VR) due to pooling of blood in lower extremities resulting in reduction in RAP, PCWP, and fall in MAP and CO, and preload, exaggerated by compression of IVC during pneumoperitoneum. These changes may be deleterious effects in patients with coronary artery insufficiency.

A steep head up causes venous stasis in the legs predisposing to deep venous thrombosis and pulmonary thromboembolic manifestation postoperatively.

ii) Respiratory changes: The changes are the opposite of head down position. FRC increases and the work of breathing decreases.

**Insufflating gas**

The ideal gas for abdominal insufflation would be physiologically inert, nonflammable, inexpensive, easily acquired, relatively absorbable by abdominal tissue and soluble in blood so that it allows pulmonary excretion and thereby minimizes potentially life-threatening effects if embolized into the venous vasculature. At the initial stages laparoscopists used only air and met with complications like air embolism, physiological trespasses like pneumothorax, pneumomediastinum, surgical emphysema. Various gases like nitrogen (air), O₂, N₂O, CO₂, helium, argon, etc have been tried. Still the ideal agent is yet to be discovered.

Zollikofer from Switzerland first used CO₂ insufflation in 1924. CO₂ is the insufflating gas of choice because of its high solubility in blood with low risk of venous embolism, non-inflammability (safety during electrocautery and laser surgery), its capability of pulmonary excretion, low cost, relatively inert, rapidly buffered by HCO₃ in blood and readily availability despite having the risk of producing hypercarbia due to its rapid absorption by abdominal viscera and tissue.

**Body's response to increased intra abdominal pressure (IAP) following pneumoperitoneum**

Pneumoperitoneum is created and maintained by insufflating gas (Initial flow, 1-1.5L/min, then higher flow rate, 2 - 3L/min) through Veress needle into the peritoneal cavity. A "Hasson" minilaparotomy technique has also been advocated for pneumoperitoneum creation to avoid injuries associated with blind Veress needle and trocar insertion. Once the pneumoperitoneum is established, the gas flow rate is reduced to maintain IAP usually at 10-15mmHg (range 5-20mmHg). About 4L of the total gas volume (range 3-5L) is required to achieve IAP of 8-12mmHg. This is necessary to create the space to visualize the surgical area through the laparoscope. The overall pressure on the diaphragm amounts to a force of approximately 50 kg in the trendelenberg position. When gas is insufflated into the peritoneal cavity, there are two immediate effects: IAP is raised to a level depending on the gas volume and cavity compliance and secondly gaseous interchange occurs across the peritoneum. Pneumoperitoneum may be
avoided by using special surgical retractors or subcutaneous wiring to lift the abdominal wall although exposure is inferior to that achieved with pneumoperitoneum. Cardiovascular, respiratory and renal changes are common and vary in degree of severity based on the length and complexity of surgery, patient’s age and his or her cardiopulmonary status.

1. CVS changes

The mechanism by which laparoscopy causes cardiovascular effects is not clearly delineated but may depend partly from two main factors: neurohumoral response following increased IAP, and hypercarbia and the subsequent acidosis.

**Neurohumoral response**

Neurohumoral response increases vasopressin partly from $1.5 \pm 0.5$ to $12.3 \pm 47$ pmol/L and later catecholamines following increased IAP. Vasopressin (Anti-diuretic hormone, ADH) causes the muscular layer of arterioles (i.e. Tunica media vasorum) to contract. The rise in vasopressin tended to parallel temporally increases in systemic vascular resistance (SVR) and blood pressure whereas elevated concentrations of catecholamines occurred later in the surgery. IV clonidine given before insufflation significantly attenuate some of these hemodynamic changes. However, renin-angiotensin-aldosterone system is also involved. The most important mechanism of the neurohumoral response of the vasopressin and rennin-angiotensin-aldosterone system is the sympathetic stress response including vagal reflexes. The increased IAP also leads to a mechanical impairment of the VR leading to an increase in venous pressure of the lower extremity while decreasing the cardiac preload. Depending on the extent of above mentioned mechanisms there will be an increase in SVR and pulmonary vascular resistance resulting in an increased afterload. The development of hemodynamic changes depends on the functional reserve of the heart. There may be a decrease in cardiac output and hypotension without an increase in the heart rate.

Other factors includes the positioning of the patient, preoperative cardiorespiratory status, intravascular volume and anesthetic agents employed.

Reflex increase in vagal tone due to overstretching of the peritoneum may produce bradycardia and even asystole and death, aggravated by lighter plane of anesthesia, patient on ß-blocker, stimulation of tracheal tube during bipolar electro-cauterization and CO2 embolization. In 0.5% of healthy patients, however, bradycardia and asystole can occur during CO2 insufflation and pneumoperitoneum. Although the exact mechanism for this response and why only certain patients experience bradycardia remains topics of continued research, it is believed that direct pressure on the vagus nerve causes a stimulatory parasympathetic effect that leads to a drop in heart rate. Hyperacarbria can also exacerbate arrhythmias. The threshold pressure that produces minimal effects on haemodynamic function is 12mmHg.

**Hypercarbia and Acidosis**

CO2 is highly soluble and therefore is very rapidly absorbed from the peritoneal cavity and retroperitoneal space into circulation. Because absorbed CO2 can only be excreted through the lungs, hypercarbia can only be avoided by a compensatory hyperventilation by increasing the tidal volume of ventilation in anesthetized patients. Hypercarbia can develop as a result of a highly increased peritoneal absorption of CO2 and an insufficiently increased exhaustion of CO2. Absorption of CO2 is increased particularly during prolonged surgery using high intra-abdominal pressure. Exhaustion of CO2 is reduced in patients with compromised cardiopulmonary function and restricted CO2 clearance. Also, the compensatory hyperventilation is impeded by the Trendelenburg position or a high intra-abdominal pressure, which cause a cephalad displacement of the diaphragm (resulting in reduction of lung volumes) and a restriction in diaphragmatic mobility. In these conditions, severe hypercarbia can develop despite aggressive hyperventilation. It should be stressed that intra-abdominal pressure has a major role in the development of hypercarbia since it both increases the absorption and decreases the exhaustion of CO2.

Hypercarbia and acidosis can cause hemodynamic changes by direct action on the cardiovascular system and by an indirect action
through sympathoadrenal stimulation.\textsuperscript{4,5} The direct effect of carbon dioxide and acidosis can lead to decreased cardiac contractility, sensibilization of myocardium to the arrhythmogenic effects of catecholamines and systemic vasodilatation. The centrally mediated, autonomic effects of hypercarbia lead to a widespread sympathetic stimulation resulting in tachycardia, hypertension and vasoconstriction counteracting the direct vasodilatory effect. Attempting to compensate by increasing the TV/RR will increase the mean thoracic pressure, further hindering VR and increasing mean pulmonary artery pressure. These effects can prove particularly challenging in patients with restrictive lung disease, impaired cardiac function or intravascular volume depletion.

**Clinical studies of hemodynamic changes:**
A biphasic change in CO is produced (CO elevated initially, then decreased). Upto 10mmHg of IAP, the cardiac filling pressures are unchanged or elevated and CO improves. Most of these studies reported increased SVR and pulmonary vascular resistance and reduction of cardiac index (CI) when laparoscopy was performed at about 15 mm Hg and head up tilt 10°. Joris et al\textsuperscript{6} using invasive monitoring, observed a significant increase in mean arterial pressure (MAP) (35%) after peritoneal insufflations, along with an increase of SVR (65%) and pulmonary vascular resistance (90%), and a decrease in CI (20%), while the PCWP and CVP increased. The decrease in CI can be partly explained by an increase in SVR. CI can be reduced by 35-40% after induction of anesthesia and rT positioning, and further reduced to 50% of its preoperative value 5min after the beginning of CO\textsubscript{2} insufflation. The CI gradually improved 10min of CO\textsubscript{2} insufflation. This biphasic change in hemodynamic has been supported by many studies whereas some investigators commented an unchanged CI during CO\textsubscript{2} insufflation. The mechanism by which biphasic changes in CO has been explained as a) it forces blood out of the abdominal organs (splanchnic venous bed) and IVC into the central venous reservoir thereby increased central BV and hence CO, b) with further increased in IAP, there is peripheral pooling of blood in the lower extremities and pelvic region, thereby tends to decrease the VR and CO. However, higher insufflation pressure (>18mmHg) tends to collapse the major abdominal vessels (particularly IVC) which decreases VR and leads to a drop in preload and CO in some patients. Transesophageal Echocardiography (TEE) has shown that there is marked decrease in left ventricular end diastolic. These hemodynamic changes are well tolerated by healthy individuals but may have deleterious consequences in patients with cardiovascular disease. The Trendelenburg position attenuated this increase while rT position aggravates it.

Using lower insufflation pressures, CVS changes were milder and transient. Three minutes after the onset of pneumoperitoneum at the pressure of 8-12 mm Hg, Branche et al\textsuperscript{7} observed a 25.7% increase in MAP, a 49% increase in left ventricular end-systolic wall stress (a measure of left ventricular afterload) and a 17% decrease in fractional area shortening (a measure of left ventricular function-contractility). All measured variables returned to preinsufflation values after 30 min of pneumoperitoneum and thereafter were no longer significantly affected by postural changes (10° head-up position) or pneumoperitoneum exsufflation.

Minimal to no changes in cardiac conduction are usually caused by pneumoperitoneum if halothane is avoided for maintenance of anesthesia. Halothane is associated with ventricular arrhythmogenesis if administered in the presence of hypercarbia, not an infrequent event during CO\textsubscript{2} insufflation. Although rare, traction on peritoneal tissue can enhance efferent vagal traffic to the sinus node and slow or abolish spontenous rhythm. Little data are available regarding the effects of pneumoperitoneum on other indices of cardiac conduction such as dromotropism and repolarization.

2. Respiratory changes
The increased IAP following pneumoperitoneum leads to cephalad displacement of the diaphragm which results in reduced lung
volumes (TV, FRC, FEV₁, VC, TLV), and thoraco-pulmonary compliance (35-40%), increased peak airway pressure and risk of barotraumas during IPPV, and an inadvertent right mainstem bronchial intubation particularly in Trendelenburg position. This decreased compliance leads to an increased in the work of breathing. There is chances of opening of embryonal channels between the peritoneal cavity and the pleural and pericardial sacs which may cause pneumothorax, pneumomediastium and pneumopericardium. The cephalic shift results in early closure of small airways leading to intraoperative atelectasis with a decrease in FRC. Uneven distribution of ventilation to non-dependent parts of the lungs (increases in less ventilated alveoli) produces ventilation perfusion mismatch, elevated dead space, intrapulmonary shunting, hypoxia, hypercarbia and atelectasis predispose to PO chest infections. This is manifested by widening of the alveolar-arterial partial pressure of O₂ difference (A-aDO₂). PaCO₂/PETCO₂ increases about 15% to 25% usually reflected to capnography. Increased in minute volume (10-25%) is required to maintain a constant PETCO₂ concentration and prevent occurrence of a respiratory acidosis (pH-7.30) that would otherwise occur. Disproportionate increased of PaCO₂/PETCO₂ (>25%) needs further search for various causes like cardiorespiratory compromise, subcutaneous emphysema, endobronchial intubation, pneumothorax and pulmonary embolism.

Depending upon absorption of CO₂ from peritoneal surface, retroperitoneal space, impairment of pulmonary ventilation, abdominal distension and patient position, an IAP of 15 mmHg raises the PaCO₂ by 10mmHg (PETCO₂ -10mmHg), the PACO₂ by 4mmHg and decreased lung compliance by 25%. During carboxyperitoneum, both PaCO₂ and PaCO₂ increases progressively (time dependent) to reach a plateau 15-20 min (range 10-30 min) after the insufflation (similar to the phasic cardiac response). This occurs both in head up and head down positions in patients with controlled ventilation, the correction of the increased CO₂ and respiratory acidosis can be made by increasing minute ventilation (10-25%) (increasing RR and / or TV 12-15mL/kg) in order to prevent progressive alveolar atelectasis and hypoxemia and to allow CO₂ elimination but will inevitably lead to some increased in airway. Both PETCO₂ and pulmonary CO₂ elimination continued to increase slowly throughout CO₂ insufflation. Although ventilation with PEEP significantly improves pulmonary gas exchange and preserves arterial oxygenation during prolonged pneumoperitoneum, PEEP in the presence of elevated IAP increases the intrathoracic pressure (ITP) and produces marked reduction in CO. A modern ventilation technique is the 'alveolar recruitment strategy', consisting of manual ventilation to an airway pressure of 40 cm H₂O for 10 breaths over 1 min, followed by usual mechanical ventilation with mild PEEP (5cm H₂O) to improves arterial oxygenation intraoperatively during laparoscopy, without clinical cardiovascular compromise or respiratory complications. Since up to 120 liters of CO₂ can be stored in the human body during pneumoperitoneum, a prolonged mechanical ventilation is needed postoperatively in some cases until CO₂ is eliminated completely. If the ventilation is not controlled, these changes are primarily mitigated by a more frequent RR but PETCO₂ concentrations still rise. However, in ASA Grade III or IV patients, PaCO₂ may remain elevated (about 3-fold more than that determined in ASA I patient) despite adjusting minute ventilation to normalize PETCO₂. Preoperative evaluation with pulmonary function tests demonstrating FEV less than 70% of predicted values, low VC, high risk ASA and diffusion defects less than 80% of predicted values can identify patients at risk of developing hypercarbia and respiratory acidosis following pneumoperitoneum. Significant variations of mean gradients of arterial - PETCO₂ is seen in patients with COPD, morbid obesity and congenital cardiac disease.

In patients with interstitial pulmonary disease or COPD, poor CO₂ diffusion and elimination may lead to significant and catastrophic increases of PCO₂. PETCO₂ measurements are unreliable and tend to underestimate the true PCO₂ in this population because of impaired gas exchange. Periodic arterial blood gas
(ABG) measurements should be obtained and in the event that \( \text{CO}_2 \) can not be quickly eliminated, pneumoperitoneum or pneumoretroperitoneum should be relieved immediately. Once \( \text{PCO}_2 \) has fallen into the acceptable range, \( \text{CO}_2 \) insufflation can be resumed and the laparoscopic procedure continued.

3. Embolism

The chance of thromboembolism is more in patients undergoing long laparoscopic procedures in the rT position. At least two factors in Virchows triad are affected (venous stasis and hypercogulability) during increase in IAP. Doppler studies showed decrease in femoral blood flow with increase IAP and there is no adaptation during prolonged surgery. At IAP >14mmHg, rT position, obesity, pelvic surgery and prolonged surgery reduce venous blood flow in the lower extremities thereby increasing chances of thromboembolism.

4. Renal and splanchnic blood flow

A pneumoperitoneum induces important changes in the physiology of the kidneys. The most common result is oliguria. The main causes of oliguria during laparoscopy are:

i) Direct mechanical compression of renal arteries, veins and parenchyma.

ii) The vicious cycle of reduced renal perfusion → activation of renin-angiotensin aldosterone system → renal cortical vasoconstriction

iii) Increased \( \text{ADH(Vasopressin)} \)

iv) Elevation of endothelin

v) Reduced \( \text{CO} \)

With desufflation, these mediators return to baseline levels, and a post-desufflation diuresis is generally noted in the following hours. Renal homeostasis is re-established within 24 hours after surgery with normalization of serum and urinary creatinine and electrolytes.

Renal and hepatic blood flow may be influenced by IAP (physical pressure of pneumoperitoneum), humoral mediators such as renin, hypercarbia and patient position. An IAP of >20 mmHg reduces renal and mesenteric blood flow. There is an overall reduction of blood supply to all the organs except the adrenal glands. The RBF and GFR decrease because of an increase in renal vascular resistance, reduced glomerular filtration gradient and reduced \( \text{CO} \). The renal effects are mild to negligible when the IAP is less than 10 mm Hg. Head-up position and IAP from 12 to 15mmHg compromised hepatic and renal blood flow in animal study. The functional consequence of the diminished blood flow(cortical renal flow decreases by 28%, medullar renal flow decreases by 31%, GFR decreases to 18-31% of normal values) to kidneys resulted in a urinary output of only 0.01±0.03ml/kg/h (63% to 64%), compared with 0.85±0.4ml/kg/h in patients undergoing laparoscopic surgery using \( \text{CO}_2 \) pneumoperitoneum or an abdominal wall retractor, respectively. There is also reduction of creatinine clearance and sodium excretion. This is a functional (prerenal) acute renal failure, which is generally reversible after 2 h postoperatively. The greater concern is to avoid over-resuscitation, fluid overload, pulmonary edema, and exacerbation of congestive heart failure. Prolonged renal hypoperfusion carries the risk for acute tubular necrosis and its consequences. One must keep in mind the possibility of renal, hepatic and intestinal failure after laparoscopic procedures. Some prophylactic actions are available and can easily be taken before acute tubular necrosis occurs.

Methods for maintaining renal perfusion:

i) Intravascular volume loading should be done before and during pneumoperitoneum. In an effort to maintain renal perfusion and minimize possible deleterious effects on graft function, some investigators have suggested the use of isotonic and hypertonic intravascular volume expansion for transplant cases. An alternative to volume expansion is to decrease IAP as much as visualization will allow.

ii) Low dose dopamine 2 \( \mu \)g/kg/min can prevent renal dysfunction usually associated with long-lasting laparoscopic procedures and higher pressures of pneumoperitoneum (~15 mm Hg).

iii) Urine output is significantly higher when insufflation of gas at body temperature is used as compared with room temperature \( \text{CO}_2 \) insufflation. Warm insufflation probably causes a local renal vasodilation and may be beneficial.
to patients with borderline renal function.\textsuperscript{16} iv) Esmolol inhibits the release of renin and blunts the pressor response to induction and maintenance of pneumoperitoneum. Therefore, it may protect the kidneys against renal ischemia during laparoscopy.\textsuperscript{17} v) Non-steroidal anti-inflammatory drugs (NSAIDs), widely used for pain management, can cause renal medullary vasoconstriction that may induce acute tubular necrosis if added to the previous vasoconstriction caused by pneumo-peritoneum.\textsuperscript{18} Therefore, NSAIDs, both the 'older' ones and the new selective COX-2 inhibitors (selective inhibitors of cyclooxygenase-2 enzyme) should be avoided preoperatively in patients with impaired renal function or renal diseases.

High risk of regurgitation and aspiration (acid) of gastric contents has been reported during laparoscopic procedures. Several factors that predispose to regurgitation are steep head down tilt, IAP during insufflation of intraperitoneal gas and mechanical pressure exerted on the abdomen by the surgical team. However, risk of gastric regurgitation from IAP during insufflation is usually minimized due to increased lower esophageal sphincter tone.

Studies in rats have shown a decrease in splanchnic macro- and micro-circulation depending on the amount of intra-abdominal pressure.\textsuperscript{19} An increase of 5 mm Hg, from 10 to 15 mm Hg of the intra-abdominal pressure resulted in a blood flow decrease to the stomach (40-54%), jejunum (32%), colon (44%), liver (39%), and peritoneum (60%).\textsuperscript{20} The fall in blood flow to these organs may be due to release of hormones (catecholamines, angiotensin and vasopressin), mechanical compression on abdominal organs and rT position.

Few studies showed increased levels of aminotransferase (alanine aminotransferase, aspartate aminotransferase) and also of alcohol dehydrogenase and glutathione S-transferase but the phenomenon is transient as these enzymes returned to normal values within 1-3 days.\textsuperscript{21} These changes are clinically silent in patients with a normal liver function. Even in selected patients of Child-Pugh classes A and B with compensated cirrhosis some laparoscopic procedures (cholecystectomy, appendectomy, splenectomy) seem to be safe, in any case safer than the 'open' procedures.\textsuperscript{22}

5. Temperature
There is a 0.3°C fall in core temperature for every 50 L flow of CO\textsubscript{2} due to the continuous flow of dry gases over the peritoneal surfaces under pressure because of the Joule-Thompson effect (sudden expansion of gas), higher flow rate and leakage through the ports. If the gas used is dried, the heat expenditure to humidify the dry gas is much more than just warming dry CO\textsubscript{2}. Insufflation of gas at body temperature is recommended.

6. Hormonal effects
Laparoscopy elicits a classic stress response but a lesser degree as evidenced by the increased in the concentrations of plasma ACTH, cortisol, epinephrine, norepinephrine, glucagons, insulin, dopamine and renin.

7. CNS
Laparoscopy causes increase in ICP. Two mechanisms have been suggested to account for this rise in ICP: i) impaired venous return of lumbar venous plexus and head caused by increase in IAP, ITP and Trendelenburg positioning and ii) increase intracranial flow due to elevated PaCO\textsubscript{2} after abdominal insufflation. Safety of laparoscopy in patient with pre-existing elevated ICP has been reported. However, more detailed human studies are required.

8. IOP
Increase in IAP compresses IVC and increases lumbar spinal pressure by reducing drainage from the lumbar plexus, then increases IOP.

9. Pediatric patient
In pediatric patient P\textsubscript{E}CO\textsubscript{2} rises more rapidly and achieves plateau values sooner in younger (11-24 months of age) versus older (5-14 yr of age) children during CO\textsubscript{2} insufflation.\textsuperscript{23} Tobias and coauthors\textsuperscript{24} noted small change in P\textsubscript{E}CO\textsubscript{2} (32±3 to 35±5 mmHg) and peak inflating pressure (20±3 to 23±3 cm H\textsubscript{2}O) after insufflation during brief laparoscopic inspection (15 min) of the peritoneum. Changes in BP, HR, RR and TV are not always consistent but
appear to be at least qualitatively similar to those in adult patients. In another study, P\text{et}CO\text{2} concentration overestimate PaCO\text{2} in longer laparoscopic procedures.

Insufflation of CO\text{2} is limited to a pressure of 8-15 mm Hg (average 10mmHg) in children to minimize diaphragmatic splinting. Gasless laparoscopy is achievable by lifting the abdominal wall with special retractors or subcutaneous wiring.

With increases in IAP, the diaphragm is pushed relatively more cephalad in children, thereby decreasing FRC. Diaphragm mobility decreases significantly as does overall respiratory efficiency. Both respiratory rate and peak airway pressures will increase, and the respiratory changes appear to be more significant with intraperitoneal than extraperitoneal insufflation. From a metabolic standpoint, CO\text{2} absorption is much more efficient in children due to a relatively greater absorptive surface-to-weight ratio. To prevent hypercarbia, minute ventilation should be increased, with close monitoring of P\text{et}CO\text{2} and arterial oxygenation in longer cases.

Urologic laparoscopy in the pediatric population is generally well tolerated. From a cardiac perspective, a similar IAP-dependent physiologic response can be anticipated. When IAP is maintained at 10 to 12 mm Hg or less, clinically significant hemodynamic compromise is generally not observed; although increases in SVR (162%) and decreases in cardiac performance (67%) have been reported at pressures of 10 mm Hg. As with adults, bradycardia and asystole can occur during gas insufflation from vagal nerve stimulation. Children typically have a higher resting vagal tone. Therefore, it is advisable to minimize IAP if visibility allows because lower IAP is associated with fewer cardiac effects and initiating pneumoperitoneum at a lower insufflation rate may be warranted.

Low complication rate (1-2%) of laparoscopic surgery in children has been reported. Complications are more or less same as in adults.

**Anaesthetic considerations**

Careful pre-operative assessment is required focusing on cardiac and respiratory reserve, liver and renal function because these organs may be affected by the increase IAP. Medical illness such as diabetes, hypertension, asthma, and hypothyroidism need to be optimally controlled before surgery.

In patients with pulmonary and cardiac disease, specialty consultation is generally necessary. The cardiac and pulmonary, liver and renal function should be carefully evaluated and optimized so that the best preoperative condition is achieved and the operative risk is acceptable. Concomitant use of cardiotoxic, hepatotoxic and nephrotoxic drugs should be avoided.

Although reported safety of laparoscopy in some neurosurgical procedures in patients with pre-existing elevated ICP, there is still the possibility of laparoscopy causing increase in ICP.

Patients with distorted abdominal anatomy (e.g. obesity, prior abdominal surgery with adhesions) are at higher risk for vessel or organ damage or puncture during insertion of Veress needle or larger trocar that encases the video camera. The experience and the skill of the surgeons must be counted.

Conversion to laparotomy is always a possibility and must be taken into account during pre-anaesthetic assessment.

Laboratory investigation of a patient should be based on the evaluation of the patient (history and physical examination). Electrolyte and creatinine analysis, coagulation studies, chemistry panels including LFT, ECG, and chest radiographic films are advised. A blood sample should be sent to the blood bank for cross-match. For procedures in which blood loss is not anticipated, a type and screen is sufficient. Autologous blood use should be encouraged if the patient is in good general health.

Prophylactic antibiotics should be given specially patients with valvular heart disease, a history of endocarditis, a vascular graft, or implanted devices.

**Premedication**

Premedication needs meticulous preparation keeping in mind the onset and duration of action of drugs since many laparoscopic procedures are now conducted on day care basis.
Preoperative visits are clearly helpful to alleviating anxiety. In addition to psychological preparation, patients also benefit from premedication. A short acting anxiolytic, benzodiazepine like midazolam allays anxiety and ensures a rapid recovery.

An antiemetic like ondansetron (4-8mg IV), granisetron (40µg/kg BW IV), dexamethasone (8mg IV) reduces postoperative nausea and vomiting (PONV). A gastrokinetic such as metoclopramide (10mg IV, 1-3min prior to induction of anesthesia) hastens gastric emptying and increased lower esophageal tone. An H₂ antagonist (ranitidine 50mg IV 1-2h before induction of anesthesia) reduces the volume and raised pH of gastric secretions. Premedication with oral omeprazole, 40mg at night and in the morning also appears to be highly effective in patients with laparoscopic surgeries. Anticholinergic like glycopyrrolate 0.1-0.2mg IM 1h prior to induction helps to reduce airway secretion. Pre-emptic analgesia (multimodal analgesic) is achieved with parenteral NSAIDS and opioids. Deep vein thrombosis (DVT) prophylaxis may be recommended.

**Monitoring**

Minimum mandatory monitoring like HR, ECG, NIBP, pulse-oximetry (SPO₂), continuous capnography/capnometry (P₄EtCO₂) and temperature probe should be used. P₄EtCO₂ is most commonly used as a noninvasive substitute for PaCO₂ in the evaluation of the adequacy of ventilation during LC. When pneumoperitoneum occurs, the PaCO₂ increases and may require an increased minute ventilation (12-16%) to maintain normal PaCO₂ close to preinduction levels. However, P₄EtCO₂ may not be a satisfactory noninvasive index of PaCO₂ if it exceeded 41 mmHg and if large volumes of CO₂ insufflated. But P₄EtCO₂ proved to be a reasonable approximation of PaCO₂ in those patients free from cardio-pulmonary disease. In contrast, patients with preoperative cardio-pulmonary disease may demonstrate significant increases in PaCO₂ not reflected by similar increases in P₄EtCO₂ during insufflation. PaCO₂ may be underestimated by P₄EtCO₂ if there is a reduction in CO or an increased in V/Q mismatch, and occasionally P₄EtCO₂ may overestimate PaCO₂. In patients with cardiopulmonary disease, it would seem prudent to monitor PaCO₂ levels at times during the procedure to avoid problems with hypercarbia and acidosis.

Patients with reduced cardiorespiratory reserve (ASA grade III / IV) will require invasive hemodynamic techniques such as arterial line, BP, TEE, periodic ABG measurement, PCWP, CVP and estimation of perfusion via central venous oxygenation in order to monitor the cardiovascular response to insufflation and institute therapy. Because the CO is inversely proportional to the insufflation pressure in the abdomen, gradual insufflation should be monitored by the anesthesiologists and a limit of 8-12 mmHg set as maximal inflationary pressure. Limiting the rT tilt may attenuate the reduction in CO during pneumoperitoneum. Significant hemodynamic compromise, refractory persistent hypercarbia, acidosis, and/or a reduction in SvO₂ may necessitate exsufflation of the pneumoperitoneum or lowering of the insufflation pressure or conversion to open procedure. CO can be monitored with pulmonary artery catheters or the less invasive technique such esophageal Doppler.

**Anaesthetic technique**

Depending on the duration and type of surgeries, laparoscopic procedures can be performed under general, regional (epidural or spinal anesthesia or combined spinal-epidural, CSE) or local anesthesia (infiltration of local anesthetic with IV sedative).

**General anaesthesia:**

General anesthesia (IV induction followed by muscle relaxant, cuff endotracheal intubation and controlled ventilation - gold standard technique) is usually preferred because of patient discomfort associated with creation of the pneumoperitoneum and the extent of position changes associated with the procedure. During pneumoperitoneum, controlled ventilation must be adjusted to maintain P₄EtCO₂ at approximately 35mmHg by increasing minute ventilation by 10-25%.

Tracheal intubation with positive pressure ventilation under GA is usually favored for many reasons: 1) it protect airway and prevent the risk of regurgitation and acid aspiration.
from increase IAP during insufflation. Although operations like laparoscopic gastrostomy, jejunostomy, herniorrhaphy, gynecological and pelvic surgeries and other minimal procedures have been performed using local or RA combined with IV sedative, chances of aspiration of gastric contents is very high with these patients than GA 2) Increase in IAP and Trendelenburg positioning hinders spontaneous breathing and may compromise respiratory exchange. There lies the necessity for controlled ventilation at high TV which are used to prevent hypercarbia and to reduce atelectasis including depression of ventilation by anesthetic agents, absorption of CO₂ from the peritoneal cavity and mechanical impairment of ventilation by pneumoperitoneum and the initial steep Trendelenburg position. The obese patient would also benefit from intubation to decrease the likelihood of hypoxemia, hypercarbia and aspiration. PEEP may be applied to reduce basal atelectasis. Airway pressure should be carefully monitored and vigilance for pneumothorax maintained. The relatively high peak inspiratory pressure required because of the pneumoperitoneum 3) the need for neuromuscular blockade (muscular relaxation and immobile operative fields) during surgery to allow lower insufflation pressure provide better visualization and aids surgeons to performed a rapid safe procedure without coughing, retching and unexpected patient movement 4) CO₂ insufflates the entire abdomen including the inferior aspect of the diaphragm and may cause significant discomfort or pain as the phrenic nerves originate from the nerve roots of 3rd,4th and 5th cervical vertebrae, diaphragmatic pain is difficult to treat with local or RA. Likewise, anesthesia for manipulation of abdominal organs and peritoneal traction may be difficult to achieve using local or RA. 5) skill and efficiency of the surgeon may be necessary to complete a laparoscopic procedure in the timely manner necessary for patients experiencing laparoscopy under LA or RA. 6) the placement of an orogastric or nasogastric tube and urinary catheters to empty the stomach or bladder is an additional discomfort that may be avoided by GA and minimize the risk of visceral perforation during trocar introduction and optimizise visualization. Preloading with crystalloid solution is recommended to prevent the haemodynamic changes during pneumoperitoneum. Atropine may be administered at induction to prevent bradycardia.

Any modern IV or volatile anesthetics (such as propofol, isoflurane, sevoflurane and desflurane) may be used to maintain anesthesia, with the exceptions of halothane and N₂O. Practically, balanced anesthetic technique with O₂, N₂O, volatile anesthetic agents, relaxants, NSAIDs and opioids (e.g. tramadol, butorphanol, fentanyl, remi-fentanyl, sufentanil etc.) is still applied. Inhalational anesthetics like isoflurane, sevoflurane and desflurane show least sensitivity to arrhythmias in the presence of increased catecholamines due to hypercarbia and maintain hemodynamic stability throughout the perioperative period, ensure rapid recovery with minimal PONV and therefore may be suitable agents to use during CO₂ insufflation. These agents are favoured for patients with compromised cardiac function. Because the CO₂ may increase during laparoscopy especially if the patient breathes spontaneously, cardiac arrhythmias may occur if halothane used. However, in our experience low concentration of halothane and controlled ventilation, the incidence is less. If ventilation is controlled, laparoscopy does not preclude use of halothane. Currently, spontaneous respiration is only recommended for short laparoscopic procedures. Propofol infusion is also an excellent choice for general anesthetic in the presence of raised catecholamines during insufflation. So, it can be used an alternative to volatile anesthetics. But propofol should perhaps be avoided when anesthetizing women for pronuclear-stage transfer of embryos because this anesthetic results in a lower ongoing pregnancy rate (29%) when compared with isoflurane use (54%). N₂O has been blamed to contribute to PONV and bowel distention, intra-abdominal fire (N₂O act as an oxidizing agent to fuel sources) and may expand any CO₂ emboli into the venous vasculature. N₂O may be replaced by sevoflurane and desflurane which are having blood gas solubility constant similar to N₂O and are useful alternative agents. The omission of N₂O reduced the risk of PONV by 28%. However, there is no conclusive evidence
demonstrating a clinically significant effect of N$_2$O on surgical conditions during LC or on the incidence of PO emesis. Therefore, N$_2$O may still be a useful adjuvant during GA for this procedure. Its omission in laparoscopic surgery might also increase awareness during surgery. The advent of parenteral perioperative NAIDs and the tendency for less PO pain associated with the laparoscopic approach may obviate perioperative narcotic administration.

Following induction of anesthesia the urinary bladder is decompressed and a nasogastric tube inserted to empty the stomach thereby reduces trauma to intra-abdominal contents at the time of trocar insertion and may improve laparoscopic visualization and facilitates retraction of right upper quadrants.

Patient positioning should be done gradually to avoid haemodynamic changes. The position of the endotracheal tube (ETT) should be checked after any change in position and after insufflation to prevent displacement of ETT into mainstem bronchus with subsequent inadvertent single-lung ventilation. To lessen the possibility of mainstem bronchial intubation, the depth of endotracheal intubation may be reduced by 1.5cm, the approximate cephalad displacement of the carina during pneumoperitoneum.

Use of LMA during laparoscopic surgeries remains controversial for two reasons. a) Aspiration of gastric contents has been observed during control ventilation. Because the LMA does not partition the trachea from the esophagus as cuff ETT does, gastric contents may be more likely to be aspirated. Moreover, peritoneal insufflation and Trendelenburg positioning may compress the stomach and thereby cause gastric contents to be expelled into the esophagus, with migration into the trachea. However, the possibility of tracheal aspiration is mitigated by placement in the Trendelenburg position that allows dependent drainage of gastric contents and b) If spontaneous ventilation is required, the LMA limits the maximum positive pressure to that pressure created by the seal in the posterior pharynx, about 20mmHg. Given the displacement of the diaphragm caused by the IAP, 8 to 12mmHg, positive pressure ventilation may be compromised. Report of safe use of LMA in laparoscopic surgeries has been identified except less than 0.14% of patient suffered airway regurgitation, vomiting and aspiration of gastric contents. So, use of an LMA may not be precluded by abdominal insufflation in the absence of other contraindication to LMA insertion.

The pressure points should be padded with care to prevent nerve compression injuries.

**Post-operative pain relief**

i. Local anesthetics infiltration of the port sites and local anesthetics applied directly to the operative site. ii. Pain can be quickly controlled by a systemic multimodal approach (opioids for central pain modulation, and wound infiltration with LA and NSAIDs to attenuate peripheral pain). Shoulder tip pain is reduced by setting the patient up early in recovery. Intraperitoneal (IP) administration of LA (10ml of 0.5% bupivacaine) has been reported to reduce PO shoulder pain after minor or gynecologic laparoscopic procedures. Experiences with IP local anesthetic administration after LC have ranged from significant reduction in PO pain during the first 48h with 10ml of 0.5% bupivacaine$^{27}$ to no effect in reducing PO pain, improving lung function or attenuating metabolic endocrine responses with 20ml of 0.25% bupivacaine$^{28}$.

**Recovery**

Haemodynamic monitoring should be continued into the PO period. Decreased PaO$_2$ and increased O$_2$ demand observed after laparoscopy necessitates O$_2$ administration postoperatively, even to healthy patients.

**Local anaesthesia**

Laparoscopy under local anesthesia (LA) with IV sedation has been reported to be successful. Although PO recovery is rapid, increased in the patients discomfort, diaphragmatic pain, the risk of aspiration of gastric contents and difficulty in breathing due to CO$_2$ insufflation, and difficulty in manipulation and suboptimal visualization of abdominal organs and peritoneal traction, preclude the use of this local anesthesia technique for LC. Success with local anesthesia requires a relaxed and cooperative patient, and an experienced surgeon. IAP should be as low as possible to reduce

**CME**
pain and ventilatory disturbances. The technique is largely limited to brief gynecological procedures (e.g. laparoscopic tubal sterilization) in young, healthy and motivated patients.

Regional anaesthesia

Spinal and epidural or CSE techniques presents another alternative for laparoscopic surgeries. The same disadvantages that associate with LA may also be faced in regional anesthesia (RA). Laparoscopy under RA is best suited for lower abdominal procedures. However, procedures in the upper abdomen have been managed effectively. A high level (Sensory block upto T4-T5) is necessary for upper abdominal surgical laparoscopy for complete muscle. General anesthesia would therefore be the preferred technique for this patient.

In general, local or regional anesthetic techniques have not been advocated for LC or other upper abdominal laparoscopic procedures.

Complications

Complications of laparoscopic surgeries can develop depending on IAP, the amount of CO₂ absorption, the circulatory volume of the patient, the ventilation technique used, the underlying pathologic conditions and the type of anesthesia. Anesthesiologists caring for patients in intra-operative period and PACU should maintain high degree of suspicion for inadvertent unrecognized injuries/ complications with these laparoscopic procedures. Therefore, adequate monitoring and correct management are important to prevent the development of complications.

Incidence of laparoscopy complications:

1. Hemorrhage:
Lacerated injuries of major vessels (e.g. aorta, epigastric, iliac, hypogastric, mesenteric vessels, portal vien and other vessels) may be unrecognized because of limitation of laparoscopic visualization and is usually due to the veress needle or trocars insertion, subsequent use of scissors, probes, electrocautery, ultrasonically activated (ultracision, harmonic) scalpel and lasers. Other causes of hypotension and shock (e.g. pneumothorax, gas embolism, RT position, anesthetic overdose etc.) during laparoscopy must be considered.

Management:

i. Require early recognition and management,

ii. Usually presented as unexplained profound hypotension unresponsive to fluid and mild vasopressor therapy (e.g. ephedrine) is especially concerning during laparoscopy and may be an indication for termination of the procedure or conversion to laparotomy and repair of vessels if required.

iii. Use of open technique (Hasson mini-laparotomy) with a blunt needle to reduce the incidence of perforation.

iv. To restore vascular volume with fluids, blood and blood product and establishment of additional IV lines, and to decrease depth of anesthesia.

2. Hypotension (upto 13% of laparoscopies)
Hypotension is due to IV anesthetics like thiopentone, propofol, inhalational anesthetics like halothane, isoflurane, sevoflurane, decrease volume status of the patient, sudden inflation of abdomen (> 20mmHg) with CO₂ compressing IVC, high ITP during IPPV/PEEP, vagal response, injuries to major vessels, venous embolism and hypercarbia which may induce dysrhythmias. 12.9% of patient undergoing LC developed intra-operative hypotension.

Treatment:

i. Preoperative fluid loading (10ml/kg), vasopressor therapy and vagolytic agents.

ii. Gradual induction with IV anesthetics and
supplementation of inhalational anesthetics.

iii. Slow insufflation and low IAP should be used as far as possible. Some procedures can be done at 5-7 mm Hg, but the required abdominal distension varies with surgical procedure, anatomical conditions and myorelaxation. The recommendation is to apply the lowest possible pressure level for each particular case.

iv. Intermittent pneumatic compression increases VR and cardiac preload.

v. Extreme position should be avoided since it may have an influence both on cardiac and ventilation.

vi. Explore and repair the injuries vessels as required and treatment of gas embolism.

3. Hypertension:
The risk of hemorrhagic stroke, pulmonary edema and cardiac decompensation is high following hypertensive episodes. Because of the pharmacological interventions, incidence of hypertensive episodes is rare. But its incidence seems to be higher at the beginning of insufflations, when the increasing (but still below 10 mm Hg) IAP increases the VR by reducing the BV in the splanchnic vasculature. This increased preload augments CO and arterial pressure. The situation commonly occurs in patients having sufficient intravascular volume loading, i.e. ~10 ml/kg prior to CO₂ insufflation, a loading which is nowadays standard for the prevention of hypotension.

Causes are due to light plane of anesthesia and CO₂ insufflation and hypercarbia. Other causes of hypertension must be explored.

Treatment:
a) To increase depth of anesthesia with propofol, inhalational agents, opioids-tramadol, butorphanol, fentanyl, remifentanil etc,
b) Antihypertensive agents like calcium channel blocker, β- blocker like esmolol and vasodilator like nitroglycerine are also selectively used.
c) Slow insufflation with low IAP as far as possible and correction of hypercarbia.

4. Arrhythmias(14-27% of laparoscopies):
Cardiac arrhythmias may occur during laparoscopy with CO₂.

i) Bradyarrhythmias (sinus bradycardia, nodal rhythm, atrio-ventricular dissociation and asystole):
The causes are due to increased vagus-mediated cardiovascular reflex by rapid and excessive stretching of the peritoneum at the beginning of peritoneal insufflation, during trocar insertion, or manipulation of the viscera, aggravated by lighter plane of anesthesia, patient on β-blocker, stimulation of tracheal tube during bipolar electrocauterization and CO₂ embolization. Cardiac arrest (2-20 of 1,00,000 laparoscopies) could be araised.

Among the causes of cardiac arrest, profound vasovagal response to rapid peritoneal distension and gas embolism are particularly associated with laparoscopy.

ii) Tachyarrythmias (Sinus tachycardia and ventricular extrasystoles) are also possible. There should be a distinction between sinus tachycardia and ventricular extrasystoles which are due to the release of catecholamines following CO₂ insufflation (respiratory acidosis and increased sympathetic outflow) and hypercarbia specially in the presence of halogenated anesthetic agents.

Treatment:
i. Usually transient and spontaneously resolve with the reduction of IAP.

ii. 100% O₂ hyperventilation.

iii. Elimination of stimulation(e.g. slow insufflation if possible deflation of peritoneum, avoidance of halothane in presence of hypercarbia).

iv. Pharmacological therapy of arrhythmias (e.g.use of vagolytic drug like atropine, β-blocker - esmolol) should be available.

v. To deepen plane of anesthesia, keep CO₂ in the normal range, correct hypoxia as it may contribute the occurrence of arrhythmias and treat CO₂ embolization.

5. Injuries:
Injuries to bile duct, stomach, liver, spleen uterus, urinary bladder, bowel burns and bowel gas explosions, and vessels are associated during insertion of needle and trocars.
Fulguration (thermal) and also peritonitis are possible if a viscus is perforated during trocar introduction.

Diagnosis of injury to stomach and bowel:

a) Visualization of mucosal lining after the insertion of laparoscopic,
b) Increase IAP at the beginning of pneumoperitoneum,
c) Asymptomatic distention of peritoneal cavity,
d) Aspiration of gastric particulate matter through the lumen of the needle,
e) Feculent odour if trocar enters into the large bowel,
f) Occur usually in patients with previous abdominal surgeries,

Decompression of the urinary bladder and oral/nasogastric tube insertion before surgery may reduce injuries to intra-abdominal organs. Use of "Hasson" minilaparotomy technique has also been advised for pneumoperitoneum creation to avoid injuries associated with blind Veress needle and trocar insertion.

6. Pulmonary dysfunction (persist for at least 24 h PO):
FRC, FEV₁, TLC, PEFR and VC are reduced by approximately 25%-30% following LC as opposed to a 50% reduction following open cholecystectomy. Diaphragmatic dysfunction after laparoscopic cholecystectomy may be related to diaphragmatic tension during the pneumoperitoneum through somatic afferents arising from the abdominal wall which exert an inhibitory action on phrenic nerve discharge or visceral afferents originating in GB area or residual pneumoperitoneum. Laparoscopic surgery may reduce PO pulmonary complications by avoiding the restrictive pattern of breathing that usually follows upper abdominal surgery.

Pulmonary complications are represented by hypoxemia, barotraumas, pulmonary edema and atelectasis.

Only patients with compromised cardiopulmonary function such emphysema, COPD and cardiac disease are at risk for the development of hypoxemia. If appropriate ventilation and oxygen administration are not able to reverse hypoxemia, conversion to open surgery may be required. Most of the patients with normal cardiopulmonary function will surpass these pathophysiological changes without developing hypoxemia or severe hypercapnia. Elevated airway pressures and decreased compliance could be associated with pulmonary barotrauma, which may occur as an immediate pneumothorax. Although there is chance of impairment of pulmonary function and gas exchange during laparoscopy, the recovery of pulmonary function is more rapid and the rate of pulmonary sequelae (atelectasis) or complications (pneumonia) is lower than after open surgical procedures, irrespective to the magnitude of the procedures or age of the patient.

7. Mainstem bronchial intubation:
This can be prevented if position of the ETT is checked regularly after CO₂ insufflation and every change of patient's position.

8. Subcutaneous emphysema (sc) (0.3-3.0% laparoscopic procedures):
Usually, the gas passes through any disruption of the peritoneum into the sc tissue and into the retroperitoneal tissue. Rarely, it is the consequence of inadvertent placement of trocars and direct insufflation into the sc tissue. Further extension of sc emphysema may occur on larger areas (extremities, neck) and even to the mediastinum and pleura thereby causing pneumomediastinum and pneumothorax. The reverse situation is also possible, i.e. the extension of a pneumomediastinum into the sc tissue. If there is an involvement of the neck it is also important to monitor the upper airway for obstruction. As the sc emphysema constitutes an important reservoir of CO₂ into the body, it leads to an increase in end-tidal CO₂ concentrations and therefore increased ventilation is required.

Diagnosis:

i) Crepitis in the abdominal wall and other parts of the body if generalised.
ii) Abrupt increase in EtCO₂
iii) Upper airway for obstruction if there is involvement of the neck.

Treatment:

a) Spontaneous resolution possible,
b) Discontinuance of N₂O administration, increase in ventilation, continuation of mechanical positive pressure ventilation in the immediate PO period and ABG analysis.
9. Capnothorax (pneumothorax, pneumomediastinum and pneumopericardium):
Pneumothorax could be developed from pleural tears during laparoscopic surgical procedures at the level of the gastroesophageal junction (Fundoplication, 15%), adrenalectomy and accidental diaphragmatic injuries. Other possible routes for gas to enter the thoracic cavity during pneumoperitoneum via any congenital diaphragmatic defects (e.g. foramen of Morgagni or foramen of Bochdalek) around the esophageal and aortic hiatus and via any procedure that can damage the falciform ligament (e.g. during insertion of a Veress needle), opening of embryonic channels between the peritoneal cavity and the pleural and pericardial sacs, rupture of pre-existing congenital pulmonary bullae as a result of increase alveolar inflation from increase minute ventilation, as a result of CO2 dissecting and spreading through retroperitoneum or by the extension of a sc emphysema up to pleura, resulting in pneumothorax and pneumomediastinum (e.g. after laparoscopic extraperitoneal inguinal hernia repair).

Diagnosis:

i. Increase EtCO2,

ii. Oxygen desaturation, increased airway pressure and reduced air entry, and should be confirmed by radiography,

iii. Decrease thoracopulmonary compliance,

iv. Abdominal movement of one hemidiaphragm on laparoscopic view.

Treatment:

i. Avoid thoracentesis unless necessary as spontaneous resolution occurs within 30-60 min after insufflation.

ii. Discontinuance of N2O administration, decrease in insufflation pressure and IAP and continuation of mechanical ventilation (PEEP if necessary) and adjustment of its setting.

iii. Pneumomediastinum and pneumopericardium are manifested as the above picture mostly. Usually desufflation of abdomen is adequate to relieve such complications.

10. Venous CO2 embolism (0.0014-0.6% of laparoscopies):

Embolic occurs from unintentional insufflations of gas into an open vein/tear in a vessel in the abdominal wall or peritoneal cavity during introduction of the pneumoperitoneum needle, subsequently trocar placement or later during sharp dissection or electrocautery, ultra-sonically activated (ultracision, harmonic) scalpel or lasers at the operative site and presence of pressure gradient to drive the gas from the intra-abdominal cavity into the venous vasculature.

CO2 > 1 L/min may enter the vessels before significant embolism.

Emboli may lodge in the right atrium/ventricle to form a gas lock which may impair VR and obstruct right ventricular outflow resulting in sudden CV collapse.

Emboli may also enter pulmonary circulation resulting in hypoxemia, acute pulmonary hypertension, pulmonary edema and right heart failure and CV collapse and death.

60% of symptomatic cases occur during initial insufflation.

Diagnosis:

i. Transient increase EtCO2 in early stage and decrease later due to more decreases pulmonary dead space and cardiovascular collapse.

ii. Increase pulmonary artery pressure, profound hypotension, dyspnea, hypoxia (cynosis), Mill wheel murmur on auscultation, arrhythmias or asystole and death.

iii. TEE is an extremely sensitive monitor to detect material embolized into the right heart and can identify all CO2, even those with volumes as small as 0.1mL/kg. 68% of asymptomatic patients have CO2 bubbling in the right chamber of the heart during laparoscopic cholecystectomy.

iv. Doppler techniques are the most sensitive indicators of embolic phenomena. Transcranial Doppler experiments have shown that CO2 bubbles may even reach the cerebral circulation.

Treatment:

i. Immediate cessation of CO2 insufflations, deflation of pneumoperitoneum and discontinuation of N2O.

ii. Patient turned to left lateral decubitus with head down position (Durant's
position) to allow the gas to rise into the apex of the right ventricle and prevent into the pulmonary. The Trendelenburg position is also sufficient as it has the same effect.

iii. Hyperventilation of patient and administration of 100% O₂ helps rapid CO₂ elimination. Use of PEEP to prevent paradoxical emboli remains controversial for gas emboli.

iv. Removal of air through central venous catheter, aggressive cardiopulmonary resuscitation, administration of IV fluids and catecholamine, management of arrhythmias, hyperbaric O₂ therapy and cardiopulmonary bypass.

Use of Hasson technique is recommended instead of the Veress needle because incidence of gas embolism is less with Hasson technique (0%) than the Veress needle technique (0.001%).

11. Hypercarbia:
Causes of hypercarbia are increased IAP and Trendelenburg position. Other causes of hypercarbia must be sought.

Treatment:
Hyperventilating the patient by comparatively less TV to prevent pulmonary barotraumas and greater ventilatory frequencies, and use of lower insufflation pressure as far as possible.

12. Positioning of patients:
Nerve injuries are usually due to inappropriate positioning of the patient or pressure exerted by surgical teams, hyperabduction of shoulder joint (brachial plexus injury) and during lithotomy position (perineal, femoral and external cutaneous nerves injuries). Usually spontaneous recovery but preventable if hyperabduction is avoided at the shoulder joint and placement of arms by the side of the patient in adducted position.

13. Retention of foreign bodies due to limited visualization.

14. PONV:
PONV is common (53-70% in LC). Prophylactic antiemetics like 5-HT₃-antagonist (ondasetron, 4-8mgIV, granisetron, 40µg/kg BW IV), dexamethasone (8mgIV), metochopramide (10mg IM/ IV), H₂-blocker (ranitidine, 50mgIV) and acupressure are recommended. Combination of 5-HT₃-antagonist and dexamethasone is quite effective.

15. PO pain including shoulder tip pain:
Shoulder tip pain is common in laparoscopic surgeries. Diaphragmatic peritoneal irritation produces pain which is referred to the shoulder via phrenic nerve. The pain is due to conversion of CO₂ to carbonic acid in body fluids including intrapleural which is irritant to the peritoneum and subdiaphragmatic gaseous accumulation.

Treatment:

i. Removal of all gases at the end of surgery,

ii. LA instillation in the subdiaphragmatic space, application of multimodal analgesia using NSAIDs and opioids analgesic and LA infiltration in the port sites.

iii. Sitting the patient up early in recovery.

16. Deep vein thrombosis:
Venous stasis in the lower limbs (40% reduction of femoral venous blood flow) and microendothelial injury are due to vasodilatation and platelet hyperaggregability (Virchow’s triad) are involved during pneumoperitoneum, aggravated by reverse Trendelenburg position.

Treatment:
Low molecular weight heparin, sequential compression in the intraoperative period and early ambulation are also advocated.

17. Infections: Laparoscopy increases risk of spread of infection and should be treated with antibiotics.

18. Spread of malignancy: Tumour implantation at the port site is possible.

19. Incisional hemia: Preventable if meticulous suturing and care the surgical wound are taken.

Conclusion
Laparoscopic surgical techniques have been rapidly accepted by surgeons worldwide but presents new challenges to the anesthesiologists. A thorough knowledge of the physiological changes and the advantages of keeping IAP less than 12 mm Hg and the special hazards and complications like hemorrhage, injuries to organs, CO₂ embolism, capnothorax associated with the laparoscopic techniques and vigilant monitoring particularly serial arterial blood gases and correct management are the backbone for an uneventful and complete success.
References

Low dose intrapulmonary artery rt-PA thrombolysis in a patient with massive acute pulmonary thromboembolism with history of recent cerebrovascular accident: a case report

A 59 year old female, known case of hypertension since 12 years was admitted in coronary care unit of PGIMER, Chandigarh with history of increasing shortness of breath two days prior to admission. She also had history of restlessness associated with cold and calmy skin since the morning of admission. There was history of cerebrovascular accident 10 days back with a large left parietal infarct on CT head (Fig 1). On examination, she was restless, tachypnoic (RR=40/min), pulse of 106/min, BP of 70/60 mmHg on dopamine and noradrenaline support. Chest was clear and cardiovascular examination revealed normal S1 & S2 with no murmur. On neurological examination, she was conscious, oriented with right hemiparesis and up going right plantar. Her right lower limb was swollen and tender with clinical evidence of deep vein thrombosis.

On investigation, ECG showed sinus tachycardia, normal axis with 1mm ST sagging in lead V1 to V6 with CPK-MB of 27iu/L. Echocardiography revealed dilated RA/RV, paradoxical IVS motion, mild TR (RVSP=RAP+ 28mmHg) with small LV cavity and good contractility(EF=50%). Compression USG both lower limb showed right femoro-popliteal deep vein thrombosis. An emergency CT angio chest showed saddle thrombus extending into both pulmonary arteries (Fig 2).

Patient was initially supported with IV fluid, double ionotropes, oxygen inhalation, antiplatelet and LMWH (Enoxaparin) therapy. Her condition deteriorated in spite of the treatment with falling PaO2, arterial oxygen saturation and increasing tachypnoea. She was put on mechanical ventilator with CMV mode under sedation.

In view of the intractable hypotension in spite of the optimum dose of double ionotropic agents with type 1 respiratory failure needing ventilatory support, decision for low dose intra-arterial rtPA thrombolysis was taken with the idea that it may reduce the chances of IC...
CASE REPORT

Fig 3. 6 F Pigtail catheter in pulmonary artery causing catheter fragmentation of Pulmonary thrombus followed by intrapulmonary artery administration of rtPA.

break up with 6F pigtail catheter by manual manipulation (Fig 3). A local in situ intrapulmonary artery 4 mg bolus rtPA was given followed by infusion of 46 mg in 45 min. It was followed by subcutaneous Enoxaparin therapy as her partial thromboplastin time after 2h of lysis was 46sec. A repeat Echocardiogram study next day showed improvement in RV contractility and reduction in RV size. Patient’s hemodynamic parameters gradually improved and ionotropes were tapered off by day 3. Patient had small GI bleed of about 150 ml on day one, which was treated with iv proton pump inhibitor (pantoprazole). No further recurrence of GI bleed was noted afterwards. There was no subsequent deterioration of the neurological status of the patient. She was gradually weaned off ventilator by day 5. A repeat CT head showed no evidence of IC bleed. She was planned for maintaining on oral anticoagulant treatment with warfarin with a target INR of 2 to 3. A decision for putting IVC filter was also taken to prevent further recurrence of pulmonary embolism from dislodged right lower limb DVT and was put before the patient was discharged from the hospital.

Discussion

Thrombolysis in acute pulmonary embolism is an approved modality of treatment in patients with features of RV dysfunction or hypotension with a window period of two weeks from the onset of symptoms. It results in more rapid clot dissolution than treatment with heparin alone. Thrombolytic therapy appears to reduce mortality in patients with shock due to massive PE, probably by rapidly restoring pulmonary blood flow and improving RV function. It also enhances the resolution of small peripheral emboli and reduces recurrence of PE.

FDA approved thrombolytic regimens for PE includes: 1) Streptokinase: 250,000 IU as a loading dose over 30 min, followed by 100,000 IU/h for 24h – approval in 1977. 2) Urokinase: 4,400 IU/kg as a loading dose over 10 min, followed by 4,400 IU/kg/h for 12 to 24h – approval in 1978. 3) rt-PA: 100mg as a continuous peripheral intravenous infusion over 2h – approval in 1990.

In an international multicenter randomized trial, it was found that a smaller bolus of rt-PA 0.6 mg/kg/15 min (maximum of 50mg) is safer than a larger dose administered over 2h. Local thrombolytic therapy has several potential advantages over systemic administration. First by delivering the drug directly into the pulmonary artery, local therapy might be accompanied by more rapid and or more complete clot lysis. Second, because of high local drug concentration, low dose might achieve the same degree of thrombolysis as higher systemic doses. Finally, local therapy might be accompanied by a lower risk of bleeding, especially if lower doses are used.

A randomized control trial compared peripheral intravenous and local pulmonary artery infusion of rtPA in patients with angiographically documented PE. Both routes of administration caused similar rate of lysis, bleeding and induction of a systemic lytic state. It is the only controled study comparing between these two modes of administration.

Local pharmacological thrombolysis using low doses of urokinase or rt-PA and either high-pressure intraembolic infusion or mechanical clot disruption has been investigated. In one report, six patients with contraindication to systemic thrombolysis received low-dose intraembolic thrombolysis using special catheter in a nonrandomized study, systemic fibrinolysis and bleeding did not occur, and all patients were found to have at least a 20% angiography improvement by 1h and 50 to 90%
improvement by 24h.

Various methods of catheter embolectomy and mechanical fragmentation of thrombus have been described. These catheterization methods include mechanical fragmentation of thrombus with a standard pulmonary artery catheter, clot pulverization with a rotating basket catheter, percutaneous rheolytic thrombectomy and pigtail rotational catheter embolectomy.

The present index case was taken up in the catheterization laboratory and mechanical fragmentation of thrombus was done with 6F pigtail catheter under manual manipulation.

In view of the associated large left parietal infarct with higher chances for subsequent IC bleed, low dose (50mg) intrapulmonary artery thrombolysis was given. She responded clinically by improvement in hemodynamic parameters with complete withdrawal of ionotropes by day 2. Repeat echocardiography study 24h later also showed improvement in RV function.

Recent history of cerebrovascular accident with parietal infarct is a relative contraindication for thrombolysis in patients with acute PE. However, in patients with massive PE presenting in shock with respiratory failure, the risk of IC bleed with thrombolysis is to be balanced against the worse outcome as expected without thrombolysis. This case report described such a high-risk patient who was successfully treated with low dose intra-arterial rt-PA and manual fragmentation of the thrombus with pigtail catheter.

References
A 58 year old male patient was admitted to the male ENT ward on 17th August'05 with the complaints of pain at the area of left upper molar teeth for one month and left sided headache, nasal obstruction and painful swelling of the left face followed by gradual development of nasal obstruction since the last 2 weeks. There was history of extraction of the 2 left upper molar teeth for caries teeth one month back. Patient gave history of new experience of intense irritation inside the nose and increase in swelling of the face whenever he consumed non-vegetarian food since he developed the symptoms. On examination, patient had mild fever, mild degree of proptosis with hyperemia in the left eye, swollen left side of face and tenderness of left maxillary sinus. Left nostril was found congested with crust formation and a polyp was seen at the middle meatus.

Routine hematological and biochemical investigations reports were within normal limits except the ESR was 85 mm/1st hr. ELISA test for HIV antibody was non reactive. There was no history of tuberculosis. X-ray chest PA view was normal. Contrast axial CT scan of PNS showed focal hyper attenuation in the soft tissue mass with destruction of ostium and left medial wall of maxilla (Fig 1).

Endoscopic polypectomy with uncinctomy and Caldwell-Luc operation was performed on the left side of the maxillary sinus. The maxillary sinus was found to be enlarged and filled with peanut butter and axle grease looking necrotic tissue which was curetted out. There was also erosion in the posterior wall of left maxilla, communicating with pterygo palatine fossa. There was profuse bleeding during the excision. The curetted materials were sent for staining, aerobic, anaerobic and fungal cultures for isolation and identification of the causative organisms and histopathological examination.

Microbiologically, the samples were processed by 10% KOH mount, Gram stain, Ziehl Neelsen stain, aerobic, anaerobic and fungal cultures. Fungal culture was done on two SDA (Sabouraud’s dextrose agar) media with chloramphenicol. The media were incubated at 25°C (room temperature) and 37°C for 4 weeks to isolate the dimorphic fungi.

Microscopic examinations of caseatic necrotic
tissue material in the stained films including the Z-N stain did not show the presence of any microorganism. KOH mount revealed branched septed hyphae, measuring the size of 3-6µm. Fungal culture at 37°C after 1 week revealed powdery, green colonies with the reverse being white in color. Lacto Phenol Cotton Blue (LCB) examination showed smooth conidiophores, size about 300µm with single sterigmata covering upper half of the vesicle (Fig 2).

Similar type of colony morphology was seen at 25°C but growth was seen after 2 weeks of incubation (slow growth). Finally the fungal growth was identified as Aspergillus fumigatus. Bacterial culture showed no growth after 48 hours of incubation at 37°C. Histological examination showed focal necrosis with edematous mucosa and few eosinophils (Fig 3). Histopathological diagnosis was inflammatory tissue and no evidence of malignancy.

The patient was treated with fluconazole 150mg daily for five days as soon as the positive fungal culture report comes in addition to antibiotic cover up. There was no sign of response of treatment with fluconazole. The antifungal drug was changed to amphotericin-B infusion, given in the dose of 50 mg in 5% dextrose infusion once a day after an initial sensitivity dose and repeated on every third day. A course of prednisolone was also given. After 5 doses of treatment patient responded to amphotericin-B infusion. A total of 44 doses of amphotericin-B were infused and the patient became clinically symptom free.

The left maxillary sinus was washout with normal saline for twice at the gap of one week before the patient was discharged. Mucus plugs were found in the first washing which was negative for fungal culture and the retained fluid of second washout was clear. X-ray of PNS showed reduced haziness on the affected maxillary sinus compared to previous X-ray. During the treatment period the serum creatinine level was found to be raised a little above the normal level but returned to normal level at the end of medication. The routine blood examinations and liver function tests were monitored during the treatment and were found to be within normal limits. The patient was discharged on capsule itraconazole 200mgs daily for one month with advice for follow up at one monthly interval.

Discussion

The combination of nasal polyposis, crust formation and sinus cultures yielding Aspergillus spp. was first noted in 1976 by Safirstein¹, who also observed the clinical similarity with allergic bronchopulmonary Aspergillosis (ABPA). Subsequently this disease was known as allergic fungal rhinosinusitis (AFS).

The AFS is a disease condition where the eosinophilic host responses occurred in presence of fungi within the nose and paranasal sinuses and produces slow accumulation of allergic fungal mucin in the sinus cavity. As its quantity increase, the involved paranasal sinus had manifestations of nasal polyps, expansile mucocele formation which produced bony remodeling and decalcification occurred, causing the disease to mimic invasion into adjacent anatomic spaces. This destruction often gives rise to exophthalmos, facial dysmorphia or intracranial extension without tissue invasion.² AFS responses to surgery therapy are very good eventually replaced by recurrence in the absence of ongoing therapy.²

Non-invasive Aspergillosis of the sinuses causing proptosis of the eye with bony erosion in immunocompetent person has been well documented³ in western countries. But its incidence is rare in the eastern part of our country as per available literature.

The fungal disease has been described at CT
as a rim of soft tissue attenuation of variable thickness along the bone walls of the paranasal sinuses and these findings have proved indistinguishable from those of bacterial infection or neoplastic disease. 

Initially we suspected the patient to be suffering from carcinoma of maxilla with extension in the left orbit. But the two episodes histopathological examination of excised of polypoid tissue showed inflammatory polyp and did not suggest any fungal disease.

Aspergillosis of sinuses arises as a secondary disease, superimposed upon a chronic sinusitis as described by Stammberger. In our patient also he was having caries teeth for 2 years and had started having symptoms after the teeth extraction. It indicates that the superimposed infection had occurred through root of the teeth. Patient was immuno-competent because he was not suffering from chronic diseases but the patient's general condition was poor because he was not eating properly and avoiding proteinous food due to fear from protein allergy. We supplemented with parental infusions and vitamins to build him up.

The patient was diagnosed to be a case of allergic fungal rhinosinusitis because of the presence of polyp, peanut butter and axle grease looking necrotic tissue in the large maxillary cavity, the CT scan finding, the hyphae at KOH preparation and the growth of Aspergillus fumigatus on culture which fulfilled the criteria's given by Bent and Kuhn too.

The AFS management depends on complete removal of all fungal mucin by surgery and prevention of recurrence through either immunomodulation (immunotherapy or corticosteroids) or fungistatic antimicrobials. In our case we removed the allergic fungal mucin i.e peanut butter and axle grease looking necrotic tissue from left maxillary sinus, pterygopalatine fossa and polypoid tissue from the nose endoscopically.

We treated the patient with amphotericin-B as it is said to be the drug of choice when there is documented bony invasion. A course of prednisolone with initial dose of 40mg daily in divided dose and tapered off over a period of 30 days was given for immunomodulation. Patient became completely symptom free and was discharged with advice for follow up at monthly interval because the disease is very prone to recur.

Acknowledgement:

The authors are thankful to the Director, RIMS, Imphal for allowing us to publish this case report. We also express our gratitude and love to the patient who have voluntarily agreed to take his photograph for the publication of this paper in the journal.

References

A 36 year old lady presented with the history of burns (burst of kerosene stove) leading to contractures of face, neck, chest and upper arm. The burns were 5 months old. Primary management was done by the surgical team in the ward and the patient was later referred for release of neck contracture and harvesting of split skin graft (SSG).

On examination, her vital signs were stable and systemic examination was un-remarkable. All the investigations were within normal limits. The contractures involved mainly the face, neck and chest and there was a fixed flexion deformity of the neck (chin approximated to sternum) (Fig 1). The anterior aspect of the neck was not visible. The angle of the mouths were moderately cicatrized and mouth opening was reduced (Fig 2).

She was scheduled for release of contractures of neck and SSG under general anaesthesia with controlled ventilation but direct laryngoscopy and surgical access to airway seemed impossible. So the release of the neck contracture was planned under ketamine until airway was secured.

Patient was pre-oxygenated with 100% oxygen for 5 min. Glycopyrrolate 0.2mg IV and midazolam 3mg IV were given prior to induction. Induction of anaesthesia was done with ketamine hydrochloride 100mg IV and the surgeon was informed to release the neck contracture until adequate neck extension was achieved (Fig 3). Following release of the contracture, endotracheal intubation was facilitated with atracurium in the first attempt. Anaesthesia was maintained with nitrous oxide, oxygen, non-depolarizing muscle relaxant, systemic analgesic and isoflurane using Bain’s circuit, and skin harvesting could be continued without any complications.

Discussion
Severe post burn neck contractures represent a challenge to the anaesthesiologist. The usual technique of general anaesthesia by intravenous induction and muscle relaxants would have been disastrous if the airway was not secured.

Laryngeal mask airway (LMA), Fibre-optic
laryngoscope, local tumescent anaesthesia and ketamine are few options in securing the airway in such conditions.\textsuperscript{1,2,3,4} However, inhalational induction technique, intubating LMA, a trachlite, retrograde approach and combitube may be useful. Tracheostomy and cricothyrotomy can be a lifesaving method of airway preservation.

Fibre-optic laryngoscope and laryngeal mask are expensive and may not be available in most places like ours.\textsuperscript{5} Pawan Agarwal, has conducted thirty cases of post burn neck contractures under tumescent local anaesthesia supplemented with intermittent dose of intravenous ketamine without endotracheal intubation.\textsuperscript{3} But in our case, we used ketamine to release neck contracture though chance of apnoea may occasionally occur and other procedures for skin harvesting are conducted under controlled ventilation to secure the airway, which is almost similar with the study of Jandova J and his coworkers\textsuperscript{6}. Inhalational anaesthesia and nasotracheal intubation with or without non-depolarizing muscle relaxants\textsuperscript{7} were not favourable in such conditions because of risk of epistaxis and bronchospasm. Succinylcholine was not used as the potential for excessive potassium release after burn could still occur for an indefinite period upto 6 months or longer\textsuperscript{8}. Rocuronium could be an alternative choice but we chose atracurium instead. Again retrograde intubation is not possible because of presence of massive scar in the anterior aspect of neck.

\textbf{Conclusion}

It is concluded that release of post burn neck contractures under ketamine is a safe, simple and effective method and can be used as a routine practice.

\textbf{References}

Non-immune hydrops foetalis: a case report

Y. Ajitkumar Singh, L. Ranjit Singh, M. Rameshwar Singh, Kh. Ibeyaima Devi, L. Bimolchandra Singh

Mrs. SD G P (second gravida, primipara), 30 years old with 24 weeks and 2 days pregnancy attended antenatal clinic of Obstetrics and Gynaecology department, Regional Institute of Medical Sciences, Imphal for the first time on 15th March 2006. She was from a rural area belonging to a middle level socio-economic group. Her last child birth was 1 year and 5 months ago. Her last menstrual period (LMP) was on 26th September 2005. Previous medical, surgical and obstetrical history was unremarkable and there was no history of blood transfusion. There was no history of any congenital malformation in the family.

On examination, her blood pressure (BP), temperature and pulse rate were within normal limits. Cardiovascular system (CVS), central nervous system (CNS) and chest were normal. Per abdominal examination revealed a 30 weeks size gravid uterus with an oblique lie with non audible foetal heart sound (FHS). On per vaginal examination, cervix was dilated just allowing the tip of a finger and un-effaced, vertex was at -2 station.

On investigations, routine laboratory tests were within normal limits. She shared the same blood group and Rh typing as her husband i.e. O Rh positive. Transabdominal sonography (TAS) revealed:

- A large cystic lesion measuring about 8.43cm X 10 cm in the neck region of the foetus with septation and echo free pattern (Fig 1).
- Generalized subcutaneous oedema with increased skin thickness all over the body, limbs and scalp were also observed.
- Bilateral pleural effusion and ascitis were also seen (Fig 2).
- Foetal parameters: BPD (Biparietal diameter)-19 Weeks 4 Days, HC (Head circumference) -19 Weeks 4 Days, FL (Foetal length) - 18 Weeks 4 Days, FHR (Foetal heart rate) - 146 beats per minute
- Doppler indices of the umbilical artery suggested increased placental impedance.

Supportive treatments were given and she delivered a female baby weighing 2.5 Kg. at 3.54 pm on 16th March 2006 with an Apgar score of 0/10 following induction with 0.5 mg PGE2 (Dinoprostone) gel instillation. Baby was markedly deformed (Fig 3) with multiple birth defects viz. cystic hygroma, anasarca, pericardial effusion, pleural effusion and increased skin thickness. Placenta weighed
Various chromosomal, foetal structural abnormalities and infections are the main causes of foetal hydrops. In our case foetus has cystic hygroma. Cystic hygroma was the most common structural foetal malformation in the series of Rose et al. An increase of the nuchal translucency thickness is probably the first stage of foetal hydrops. Depending on the severity of the underlying defect, the next manifestation is generalized skin oedema with eventual placental oedema, ascitis and pleural effusion. Similar ultrasound findings were observed in our case.

NIHF has become more common than immune hydrops foetalis. Mortality was of 81% and complications more frequent. So considerable emphasis must be placed on early antenatal diagnosis to achieve a precocious treatment and to improve the present poor prognosis. Rose et al diagnosed NIHF prenatally at 17.3 weeks. Unfortunately our case was diagnosed at the beginning of the third trimester because of late reporting by the patient. Serum human chorionic gonadotropin (hCG) is elevated in NIHF at second trimester but was unremarkable when NIHF presented later. Prenatal pericardial and pleural effusion or congenital anomalies carry a very poor prognosis in patients with NIHF. Maeda et al observed that albumin and/or packed red cell injection into foetal abdominal cavity was an effective procedure for in utero treatment of NIHF without pleural effusion, but none could be recovered in utero when it was associated with pleural effusion. In our case, we could not save the foetus.

Since non-immune hydrops becomes proportionately more common, radiologists should be aware that the diagnosis of ‘hydrops foetalis’ is not synonymous with ‘erythrobastosis’.

References
Leri-Weill Dyschondrosteosis: a case report

1S. Subhaschandra singh, 2W. Jatishwor, 3S. Ranjan

CASE REPORT

A 50 years old female presented with pain, deformity and limitation of movement of the wrist joints since her young adolescent age. She was short stature and married with three children. Two of the children, a son and a daughter were short stature. She was of normal intelligence. X-ray of both wrists with the forearms revealed the following findings (Fig 1 a & b) –

1. Relatively long ulna compared to radius.
2. Triangular shaped distal radius epiphysis.
3. Decreased carpal angle.
4. Wedging of the carpal bones between the deformed radius and protruding ulna.
5. Increased width between distal radius and ulna.

X-ray of both legs revealed short tibias and fibulas with relatively longer fibulas, i.e. tibio-fibular disproportion (Fig 2).

These are characteristics of “Madelung Deformity”. Short stature, normal intelligence, bilateral symmetrically involvement and children with dwarfism favored the possibility of Leri-Weill dyschondrosteosis. Mesomelic dwarfism with the presence of tibio-fibular disproportion and by exclusion of other causes of Madelung deformity, the diagnosis of Leri-Weill dyschondrosteosis was made. There were no biochemical or endocrinal abnormality detected. No genetic work up was done on this case.

Discussion

Leri-Weill dyschondrosteosis is an automasal dominant disease and a form of mesomelic skeletal dysplasia with Madelung deformity of the distal radius and ulna, proximal carpal bones and Mesomelic dwarfism, being a hallmark. As far as stature is concerned, final height in females is approximately 1.45m and in males 1.55m. There is also great variation among patients with identical mutations belonging to the same family. Females are more frequently affected than males and growth failure as well as clinical features, such as bilateral Madelung deformity, has been described as being more severe in females than in males. A female to male ratio is about 4 to 1 and female are more severely affected. SHOX gene (short stature homebox...
containing gene) defect that is haploinsufficiency due to heterozygote mutations the pseudo-autosomal SHOX gene is the main cause of Leri-Weill dyschondrosteosis. Characteristic Madelung Deformity is present in 74% of Leri-Weill dyschondrosteosis. The process of short stature and wrist deformity usually begins in adolescence with premature fusion of the medial aspect of the distal radial epiphysis, resulting in asymmetrical growth. Binder et al observed that the growth failure in Leri-Weill dyschondrosteosis occurred before the age of 6 years, partly already before birth. Growth velocity after the age of six was normal. It was also observed that the disturbance in growth was not as severe as in Turner syndrome. It was demonstrated that growth failure was observed during the first year of life with a mean height loss of 2.16 SDS in childhood, whereas pubertal growth was mildly or not affected. Furthermore, it was shown that children with a severe degree of wrist deformity were significantly shorter than those with mild deformities.

A German surgeon, Madelung first described the characteristic wrist deformity, i.e. 'Madeline Deformity' in 1878 before Leri-Weill dyschondrosteosis was described. The causes of this deformity may be - (i) post-traumatic, (ii) extension injuries of the wrist, (iii) Multiple Hereditary Exostosis, (iv) Turner Syndrome and (v) Idiopathic. Idiopathic variety is commonly bilateral than unilateral and asymmetrical in severity. There is symmetry of the bilateral wrists deformity in this index case. No history of trauma in childhood was present. No exostosis was seen in the radiographs. The prevalence of Madelung deformity is higher in dyschondrosteosis versus Turner Syndrome population. The metacarpal bones were normal in the index case, and the fourth metacarpal bone may be short in Turner Syndrome. In Leri-Weill dyschondrosteosis, there is typical Madelung deformity with limitation of motion at wrist and elbow and mesomelic dwarfism. Additional findings that may be seen in dyschondrosteosis are deformed tibial metaphysis, flattening of medial epiphysis. Skull and axial skeletal is characteristically normal. The patients taller than 25th percentile for height probably do not have dyschondrosteosis. There is reported association of Leri-Weill Dyschondrosteosis with middle ear deformity and conductive hearing loss. Tibio-fibular disproportion with tibia varum and long fibula are seen in 50% of the cases. There may be fusion of the C1 and C2 vertebrae. Increased predisposition of Hodgkin's in patients with dyschondrosteosis has been reported. There are therapeutic trials using recombinant growth hormone with variable results depending on the time of initiation of treatment.

References
Psychiatric disorders in Parkinson’s disease: an update

Th. Bihari Singh, Santa Naorem, N. Biplab Singh, Robinson Ningshen

Parkinson’s Disease (PD) is a neurodegenerative disorder involving disturbances in motor control. Over 60% of patients will experience psychiatric symptoms/disorders in the course of their illness. This review highlights recent developments in neuropsychiatric disorders in Parkinson’s disease and progressions in treatment.

Anxiety and Parkinson’s disease
Anxiety disorders have recently been reviewed1 and generalized anxiety disorder seems to be the most common and best studied in PD2. A few papers have suggested new rating scales to evaluate anxiety disorders in PD. In some cases, psychological factors such as depressive symptoms on anxiety contribute more to a low quality of life than motor symptoms.3 In PD patients, anxiety is often related to the off state, that is, more anxiety with less mobility. In many cases there is comorbidity between anxiety and depression in patients with PD and anxiety in particular is often not recognized by the physician.4 Selective serotonin reuptake inhibitor drugs are effective and generally well tolerated in patients with PD when treating mixed depression and anxiety states.5 Benzodiazepine should be avoided or only used with great caution because of detrimental effects on balance and cognitive functions.6

Depression and Parkinson’s disease
Patients with PD experience affective episodes. This was noticed by James Parkinson in the original description of the disease.6 Recently several new epidemiological achievements have been accomplished. Depression in patients with PD has been found in more than 40% in consecutive series.7,8 This was also found in Cumming's Seminal review.9 An interesting approach using logistic regression has investigated if risk factors for idiopathic depression in general are also markers for depression in PD.10 Not only does PD increase the risk for depression, but also depression is, in fact, a risk factor for PD and may in some cases be the presenting symptom of PD.11,12,13 An increased incidence of hypothyroidism in PD has been found and therefore the level of thyroid stimulating hormone and free T4 hormone should be examined in PD patients with any ‘mood’ symptom.14 Hypothyroidism should be treated with thyroid hormone replacement therapy and this will often in itself correct the mood symptoms.14 In cases of persisting symptoms an antidepressant should be added, since it has recently been shown that hypothyroidism can act as a risk factor for depression. An interesting open level randomized trial of pramipexol, administered as an antidepressant in moderately depressed patients with advanced PD and already on L-dopa treatment, clearly needs replication.15

1. Assistant Professor, Department of Psychiatry, Regional Institute of Medical Sciences (RIMS), Imphal.
2. Assistant Professor, Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal.

Corresponding author:
Th. Bihari Singh, Assistant Professor, Department of Psychiatry, RIMS, Imphal.
Pramipexole was used as an add-on drug and no patients with severe depression were included. In a neuropsychological evaluation of pramipexole, it was suggested that it may worsen cognitive function in PD patients. A Cochrane review that located 42 conducted studies concluded that only three met the criteria for meta-analysis. This only illustrates the need for clinical trials to answer the very important question of how depression should be treated in patients with PD.

Psychosis and Parkinson’s disease

Psychosis in patients with PD occurs in approximately 30%. In PD many cases of psychosis are caused by levodopa therapy and often in the form of complex visual hallucinations or, in mild cases, illusions. In most cases the patients vividly see small animals or have an ideation of presence of people in the room. This is the most frustrating experience both for the patients and spouses. Psychosis is a strong risk factor for nursing home placement. In younger patients psychosis is usually drug induced or secondary to depression. In older patients it should be remembered that psychosis could be the harbinger of dementia.

PD patients with psychosis should be treated in a three step approach. First of all it is important to identify underlying causes like urinary infection, stroke or metabolic changes that should explain a confusional state. Secondly the antiparkinsonian medication, levodopa and anticholinergic drugs, should be gradually reduced if possible. As a last resort, an antipsychotic drug should be administered to the patient. The first line of drug treatment is clozapine in moderate doses (15-50 mg/day). Placebo controlled, double blind trials have demonstrated its effectiveness in treating the psychosis in PD patients. The advantages are that it improves tremor, does not worsen motor functions in general, can be administered once daily and is safe in low doses. Side effects are sedation, orthostatic hypotension and sialorrhea. The drawbacks are the risk of blood dyscrasias and therefore specialized monitoring of white blood cell count is required. Both resperidone and olanzepine have been reported to increase motor dysfunction in patients with PD. The fourth, new generation antipsychotic drug that has been evaluated in drug trials in PD patients is quetiapine. Quetiapine seems to be less effective, less potent and less free of motor worsening in patients with PD compared with clozapine. However, quetiapine is easier to use, better tolerated and has a low risk of intolerable motor worsening. Some authors recommend quetiapine as first-line drug treatment in patients with psychosis, with clozapine as second line of treatment. Long follow-up studies are warranted and clozapine has been better studied in this respect.

Resperidone and olanzapine are recommended only if clozapine or quetiapine is not tolerated because of the risk of worsening motor functioning in PD patients on resperidone or clozapine. Other treatment modalities would be ziprasidone, ondansetron and electroconvulsive therapy. Ziprasidone is the newest atypical antipsychotic drug, but no studies have been published about its use in patients with PD. Ondansetron is an antiemetic and a selective 5-HT3 antagonist. Zoldan et al reported ondansetron improved psychotic symptoms in patients with PD, but this needs replication. Electroconvulsive therapy should only be considered when several drug therapies have been unsuccessful.

Conclusion

In conclusion, many psychiatric complications in patients with PD need to be assessed by clinicians to decide the right evaluation programme. Several recently developed treatments are available, but some need further evaluation and replication of interesting findings.

References


INSTRUCTIONS TO AUTHORS

1. General

Journal of Medical Society, is published from the Regional Institute of Medical Sciences, Lamphelpat, Imphal -795 004, India. It is published three times a year. The articles are accepted only on the condition that they are solely contributed to this journal. The Editorial Board has the right to revise the article and make changes (inhouse style) or may ask the author to rewrite. Papers presented in the various scientific meetings of the Society shall be given preference.

2. Scope

The Journal of Medical Society accepts, in English, Review articles, Original research articles, Short communications, Case reports, Early communications and Letters to the Editor. Articles of general interest on methods in medicine, medical education and update on therapeutics are also welcome.

Review articles and Educational forum: Review articles are written by the researchers of a considerable experience in the field concerned. The author should review the recent trend or the advances in that field. The major portion of above articles should deal with the up to date developments in the field in the last 3-5 years.

Full length research articles and short communications: Original work will be considered under these sections depending on the volume and quality of work.

Case Reports: It should be divided into case history and discussion with maximum of 6 references only. Illustrations/photographs and tables when included should be limited to two each.

Early communication: A manuscript will be accepted for Early communication if it merits publication. The decision of acceptance or otherwise will be communicated within four weeks of receipt of the manuscript and accepted articles will be published in the following issue.

Letters to the editor: Comment(s) on previously articles, items of current interest and brief original communications will be published.

3. Editorial policy

Manuscripts for publication will be considered on their individual merits. All manuscripts will be subjected to peer review. Normally all manuscripts will be sent to at least two reviewers and their comments along with the editorial board’s decision will be forwarded to the contributor for further action. The author may suggest more than 5 referees working in the same area for evaluating the manuscript. However, the JMS reserves the right to choose referees.

The Journal of Medical Society will insist on ethical practices in both human and animal experimentation. When investigations on human subjects are reported, evidence for approval by a local Ethics Committee must be given. The journal will not consider any paper which is ethically unacceptable.

The quotations, tables or illustrations published in other journals, books etc. should not be reproduced without the permission of the publisher or the original author. These materials must be accompanied by the written permission from the copyright owners.

Any article accepted for publication/published in the Journal of Medical Society will be the copyright of the journal.

4. Submission of the manuscript

a) Three copies of the manuscript should be submitted neatly typed or printed double spaced on a A4 size paper only on one side.

b) Manuscripts may also be submitted on a 31/2" PC diskette. The text files have to be in MS-Word or Adobe PageMaker format. The figures included as separate files and should be created using standard softwares. A hard copy (paper copy) of the manuscript must accompany the diskette, which must be clearly labeled. The label must contain the title of the manuscript and the corresponding author’s name and his affiliations, and address.

In case of any discrepancy between paper and disk versions of manuscript, the paper version will be considered for publication.

c) Final accepted version of the manuscript must be submitted on a diskette.

d) The manuscript must be submitted with a statement, signed by all authors, regarding the originally, authorship and copyright transfer.

e) Mailing Address: Three copies of the Article should be sent to the Editor, Journal of Medi
5. Preparation of the manuscript

Authors should keep their manuscripts short. Manuscripts should be typed double spaced on one side of good quality A 4 size paper. The font size should be less than 11 point. Page should be numbered beginning with the title page.

The language of manuscript must be simple and explicit.

5.1. Full length of original articles

It should be arranged into following sections:

a) Title page, b) Summary and Key words, c) Introduction, d) Material and Methods, e) Results, f) Discussion, g) Conclusion, i) References, j) Tables and k) Figures.

A word count is mandatory and should not exceed 3200.

5.1.1 Title page

It should be paginated as page 1 of the paper. It should carry title, the author's names and their affiliations, running title, address for correspondence including e-mail address and also the list of number of pages, number of figures and number of tables.

Title: Must not exceed 150 characters and should be informative and specific.

Authors and affiliations: The names of authors and their appropriate addresses should be given. Authorship should be clearly defined. Authors are required to submit a statement of the contributions made by each author.

Running title: A short running title of not more than 50 characters should be given.

Address for correspondence: The corresponding author's address should be given in the title page. The details of fax number and e-mail address should be provided.

5.1.2 Summary and key words

Summary: Must start on a new page carrying the following information: a) Title (without authors' names or affiliation), b) Summary, c) Key words, d) Running title. It should not exceed 250 words. The summary must be concise and clear, informative rather than indicative. New and important aspects must be emphasized.

The summary must be in a structured form consisting of AIMS, METHODS, RESULTS, CONCLUSION briefly explaining what was intended, done, observed and concluded. Authors should state the main conclusions clearly and not in vague statements. The conclusions and recommendations not found in the text of the article should not be given in the summary.

Key words: Provide 3-5 key words which will help readers or indexing agencies in cross indexing the study. Use terms from the latest Medical Subject Headings (MeSH) list of Index Medicus. A more general term may be used if a suitable MeSH term is not available.

5.1.3 Introduction

It should start on a new page. Essentially this section must introduce the subject and briefly say how the idea for research originated. Give a concise background of the Study. Do not review the literature extensively but provide the most recent work that has a direct bearing on the subject. Justification for research aims and objectives must be clearly mentioned without any ambiguity. The purpose of the study should be stated at the end.

5.1.4 Materials and Methods

The section should deal with the materials used and the methodology -how the work was carried out. The procedure adopted should be described in sufficient detail to allow the experiment to be interpreted and repeated by readers, if necessary. The number of subjects, the number of groups studied, the study design, sources of drugs with dosage regimen or instruments used, statistical methods and ethical aspects must be mentioned under the section. The methodology -the data collection procedure -must be described in detail. If the procedure is a commonly used one, then giving a reference (previously published) would suffice. If a method is not well known (though previously published) it is better to describe it briefly. Give explicit descriptions of modifications or new methods so that the readers can judge their accuracy, reproducibility and reliability.

The nomenclature, the source of materials and equipment used, with details of the manufacturers in parentheses, should be clearly mentioned. Drugs and chemicals should be precisely identified using their non-proprietary names or generic names. If
necessary, the proprietary or commercial name may be inserted once in parentheses. The first letter of the drug name should be in small cap (e.g. nifedipine, propranolol) but capitalized for proprietary names (e.g. Depin, Inderal). New or uncommon drug should be identified by the chemical name and structural formula.

The doses of drugs should be given as unit weight per body weight e.g. mg/kg and concentrations should be given in terms of molarity e.g. nmol or mmol.

Statistical methods: The details of statistical tests used and the level of significance should be stated. If more than one tests are used it is important to indicate which groups and parameters have been subjected to which tests.

5.1.5 Results

The results should be stated concisely without comments. It should be presented in logical sequence in the text with appropriate reference to tables and figures. The data given in tables or figures should not be presented in both tabular and graphic form. Simple data may be given in the text itself instead of figures or tables. Avoid discussions and conclusions in the result section.

5.1.6 Discussion

This section should deal with the interpretation of results, rather than recapitulation of them. It is important to discuss the new and significant observations in the light of previous work. Discuss also the weakness or pitfalls in the study. New hypotheses or recommendations can be put forth.

5.1.7 Conclusion

Avoid unqualified statements and conclusions not completely supported by the data. Conclusion must be drawn considering the strengths and weakness of the study. They must be conveyed in the last paragraph under discussion section. Make sure conclusions drawn to tally with the objectives stated in introduction.

5.1.8 Acknowledgments

It should be typed in a new page. Acknowledge only persons who have contributed to the scientific content or provided technical support may be mention.

5.1.9 References

It should begin on a new page. The number of references should normally be restricted to a maximum of 25 for a full paper. Majority of them should preferably be of articles published in the last 5 years.

Papers that have been submitted and accepted but not yet published may be included in the list of the references with the name of the journal and indicated as “In Press”. A photocopy should normally be submitted with the manuscript. Information from the manuscripts submitted but not yet accepted should not be included.

Avoid using abstracts and references. The “unpublished observations” and “personal communications” may not be used as references but may be inserted (in parentheses) in the text.

The references must be verified by the author(s) against original documents. Contributors should submit their manuscript (including references) in accordance to the “Uniform Requirement for Manuscripts Submitted to Biomedical Journals”, which can be accessed at http://www.icmje.org/index.html or N Engl J Med 1997;366:309-15.

5.1.10 Tables

Each table must be self-explanatory. It should be typed with double spaced on a separate sheet and numbered consecutively in Arabic numerals. Table should have a proper heading and each stub and column should also have subheadings. The number of observation, subjects and the units of numerical figures must be given. It is also important to mention whether the given values are mean, median, mean ± SD or mean ±t SEM. All significant results must be indicated using asterisks. The approximate position of the tables should be marked in the text. Do not use internal horizontal or vertical lines.

5.1.11 Figures

Each figure must be numbered and a short caption must be provided. For graphs and flow charts it is not necessary to submit the photographs. A manually prepared or computer drawn figure on a good quality paper is acceptable. Raw data for graphs must be submitted when article is accepted for publication. This will enable the Editorial office to draw the graph on the computer and incorporate it in the text at an appropriate place.

For other diagrams (e.g., tissue structure, ECG and instrument setup etc.), strongly contrasting black and white photographic print on a glossy paper must be submitted.

Identify each figure/diagrams on the back with a typed label which shows the number of the figure. The name of the leading author, the title of manuscript and the top side of the figure. The approxi-
mate position of each figure should be marked on the margin of the text.

Three figures per article will be printed free of charge. The authors will be charged for additional figures. The contributor must bear full cost of printing color plates if any.

Large/complex tables or figures may be submitted in “Final Print (Camera ready) Format” which will be scanned and printed as such.

5.2 Short communications

The format is same as that of full papers but the length including title and references should not exceed 1600 words plus two figures or tables or one of each. The summary should be less than 150 words and the number of references should not exceed 12.

5.3. Early communications

The manuscript should not be divided into subsections. It may contain up to 1200 words (including a maximum of 6 references) plus one simple figure or table.

5.4. Letters to Editor

It can have a maximum of 800 words (including a maximum of 4 references) plus one simple figure or table. The manuscript should not have subsections.

5.5 Review articles and Educational forum

It should contain title page. Summary (need not be in structured form) and key words. The text proper should be written under appropriate sub-headings. The authors are encouraged to use flowcharts, boxes, simple tables and figures for better presentation. The total number to text words should not exceed 6400 and the total number of figures and tables should be less than 10.

6. Revised manuscript

The authors should revise the manuscript immediately after the receipt of the comments from JMS. A note mentioning the changes incorporated in the revised text as per referee’s comments (point by point) should be sent. The revised manuscript has to be submitted in duplicate along with the annotated original paper within 2 weeks. If the revised manuscript is received 2 weeks after despatch from the Editorial Office, it will be considered as a new submission.

Calling for revision does not guarantee acceptance. The revised manuscripts that require major revision are likely to be sent to referees for evaluation. If the authors have substantial reasons that their manuscript was rejected unjustifiably, they may request for reconsideration. The correspondence in this regard should be sent in triplicate.

7. Proofs

Proofs will be sent to the corresponding author for final checking. It is the author’s responsibility to go through the proof meticulously and correct errors if any. Correction should be restricted to printer’s error only and no substantial addition/deletion should be made.

8. Reprints

Reprints must be ordered while returning the corrected page proofs.