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# Journal of the Vivekananda Institute of Medical Sciences

<table>
<thead>
<tr>
<th>Editorial</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Catheter Associated Urinary Tract Infection</strong> — Dr. Kalyan K. Sarkar</td>
<td>5</td>
</tr>
<tr>
<td><strong>Original Article:</strong></td>
<td></td>
</tr>
<tr>
<td>a) <strong>A Study of Catheter Associated Urinary Tract Infection in Intensive Care Unit of a Tertiary Care Hospital in Kolkata</strong> — Dr. Arjun Ray Dr. Jayanta Chakraborty Dr. Prabuddha Mukherjee</td>
<td>9</td>
</tr>
<tr>
<td>b) <strong>A Study on The Etiology of Ascites &amp; Incidence of Spontaneous Bacterial Peritonitis in a Tertiary Care Hospital in Kolkata</strong> — Dr. Sunetra Mondal Dr. Jayanta Chakraborty Dr. Prabuddha Mukherjee</td>
<td>16</td>
</tr>
<tr>
<td>c) <strong>Serum Homocysteine Level in Type 2 Diabetes &amp; its Relationship with Glycaemic Status: A Pilot Survey with 50 Patients</strong> — Dr. Semanti Chakraborty Dr. Jayanta Chakraborty</td>
<td>23</td>
</tr>
<tr>
<td>d) <strong>Study of Arsenic Exposure in Oral Carcinoma</strong> — Ms. Pritha Pal Dr. Ranjan Raychowdhury Dr. Ajanta Halder</td>
<td>27</td>
</tr>
<tr>
<td>e) <strong>Role of Environmental Pollution on Genetic Diseases Especially Down Syndrome</strong> — Dr. Gargi Podder Dr. Madhusnata De</td>
<td>32</td>
</tr>
<tr>
<td><strong>Review Article:</strong></td>
<td></td>
</tr>
<tr>
<td>a) <strong>Minimizing The Risk of Respiratory Distress Syndrome</strong> — Dr. Tapabrata Chatterjee Dr. Saugata Bhattacharyya</td>
<td>39</td>
</tr>
<tr>
<td>b) <strong>A Comparative Study on The Use of Intranasal Steroid Spray in Allergic Rhinitis &amp; Allergic Fungal Rhinosinusitis</strong> — Dr. Soumitra Ghosh Dr. A. Roychowdhury Dr. B. K. Roychaudhuri</td>
<td>51</td>
</tr>
<tr>
<td><strong>Case Report:</strong></td>
<td></td>
</tr>
<tr>
<td>a) <strong>Truncal Desquamation in a Case of Kawasaki Disease</strong> — Dr. S. Guha, Dr. D. Mondal Dr. S. Basu, Dr. N. Mukherjee Dr. D. Mukherjee</td>
<td>58</td>
</tr>
<tr>
<td>b) <strong>A Rare Association Between Adult Onset Still's Disease &amp; Dermatomyositis</strong> — Dr. S. N. Burman Dr. P. Chakraborty Dr. S. Mazumdar Dr. R. Rajak</td>
<td>61</td>
</tr>
<tr>
<td><strong>Pictorial CME:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Hemangioma : An Overview</strong></td>
<td>64</td>
</tr>
<tr>
<td>— Dr. Jayanta Chakraborty Dr. Debdatta Kar</td>
<td></td>
</tr>
<tr>
<td><strong>Pictorial Quiz</strong></td>
<td>68</td>
</tr>
<tr>
<td><strong>Achievement</strong></td>
<td>71</td>
</tr>
<tr>
<td><strong>Obituary</strong></td>
<td>72</td>
</tr>
</tbody>
</table>
JOURNAL OF THE
VIVEKANANDA INSTITUTE OF MEDICAL SCIENCES
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Editorial

Catheter Associated Urinary Tract Infection

In this edition of the Journal, Ray et al reported on “A study of catheter associated urinary tract infection in intensive care unit of a tertiary care hospital in Kolkata”. This is a commendable effort, given that there is paucity of data from the Indian subcontinent in this area of clinical research. This study reports on the widespread isolation of poly antimicrobial resistant urinary tract pathogens in fifty patients carrying indwelling catheters and admitted in an intensive care unit. About 36 percent of strains were betalactam sensitive. Escherichia Coli accounted for 58 percent of all isolates. This paper highlights the importance of surveillance for nosocomial urinary tract infections, and the need to avoid or reduce indwelling urethral catheterization.

Catheter associated urinary tract infections (CAUTI) account for 15 percent of infections reported by acute care hospitals\[1\]. Along with pneumonia they are the second most common form of nosocomial infection, following surgical site infections. CAUTI can have devastating implications in patient care, leading to complications such as prostatitis, epididymitis, and orchitis in males, and cystitis, pyelonephritis, gram-negative bacteremia, endocarditis, vertebral osteomyelitis, septic arthritis, endophthalmitis, and meningitis in all patients. These complications may cause severe morbidity and mortality, prolonged hospital stay and add to attendant expenses\[2,3\].

The urethral catheter allows ingress of bacteria into the urinary tract. Bacteria may enter during catheterization, around the catheter, during manipulation of the catheter and the drainage system, and may remain in the urinary tract after removal of the catheter. Mucosal injuries caused by the catheter allow colonization by bacteria, and a bio film of bacteria readily covers the surface of the catheter\[4\]. Bacterial biofilms are particularly resistant to antibiotic penetration. Daily the bacterial count increases in such a catheterized urinary tract, and within 2-4 days 10-30 percent of patients develop catheter associated asymptomatic bacteriuria (CA-ASB). More than ninety percent of patients with indwelling catheters eventually develop CA-ASB. These are potentially pathogenic bacteria and may lead to the development of symptomatic urinary tract infection (CA-UTI), sometimes progressing into explosive life threatening urosepsis. Eighty percent of nosocomial urinary tract infections are due to indwelling catheterization.

*Escherichia coli* and other enteric bacteriae from the patient’s colonic flora are most commonly responsible. *Pseudomonas* species, *Enterococcus* species, *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterobacter* species, and yeast are also common pathogens. *Proteus* and *Pseudomonas* species are the organisms most commonly associated with biofilm formation on catheters. Bacteriuria is commonest in patients who are catheterized for long periods, and where colonization of the drainage bag occurs. Single bacteria are cultured in short term catheterization associated UTIs. Beyond a month of catheterization, mixed flora are commonly cultured. Diarrhea, diabetes, absence of antibiotic
cover, female gender, renal insufficiency, errors in catheter care, catheterization late in the hospital course and immunocompromised or debilitated states are factors strongly associated with bacteriuria. Emergence of multiple drug resistant strains of bacteria is a real problem worldwide. It is important to take deliberate steps to prevent and manage catheter associated urinary tract infections. Improved management of catheter-related UTIs was approved as a National Patient Safety Goal for 2012 in the USA[5].

The 2009 Centers for Disease Control and Prevention (CDC) and Infectious Diseases society of America (IDSA) guidelines for prevention of catheter-associated urinary tract infections (CAUTIs) recommends catheter use only for appropriate indications[6,7,8]. Closed drainage of the bladder is the single most important intervention in the prevention of CAUTIs. The drainage bag should be below the level of the catheter and drainage tube. Catheter use and duration should be minimized in all patients, especially those at higher risk for catheter-associated UTI (e.g., women, elderly persons, and patients with impaired immunity). Indwelling catheters placed in patients undergoing surgery should be removed as soon as possible postoperatively. Reminder systems for early removal of catheter may be useful. Use of urinary catheters for treatment of incontinence in patients should be avoided. Clinicians should avoid using systemic antimicrobials routinely to prevent catheter-associated UTI in patients requiring either short or long-term or intermittent catheterization. Antibiotic irrigation of the bladder is not recommended, and neither is antibiotic instillation in the drainage bag. Meatal hygiene can do no harm, and maintains cleanliness, but meatal antibiotics are not useful. Alternatives to indwelling urethral catheters that are less prone to causing symptomatic infection, include, in appropriate patients, suprapubic catheters, condom drainage systems and intermittent catheterization, and these options should be always considered. 2009 IDSA guidelines recommend fortnightly change of catheters, which need to stay long term[7].

Symptoms of catheter-related urinary tract infection (UTI) generally are nonspecific. Most patients present with fever and leukocytosis, rigors, altered mental status, malaise, or lethargy with no other identified cause. Patients may complain of flank pain and have costovertebral angle tenderness. There may be associated hematuria and pelvic discomfort. Those whose catheters have been removed may complain of dysuria, urgent or frequent urination and suprapubic pain and tenderness.

Infections may be polymicrobial. Pyuria and elevated bacterial colony counts are seen in all patients in whom a catheter has been in place for more than a few days. In this situation, their presence is not synonymous with a UTI. CA-UTI in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identified source of infection along with 1000 colony-forming units (cfu)/mL or more bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral, suprapubic, or condom catheter has been removed within the previous 48 hours. If catheterization can be discontinued, the culture can be obtained in a voided midstream urine specimen. If an indwelling catheter has been in place for longer than 2 weeks at the onset of the
UTI and is still indicated, it should be replaced, and the urine culture should be obtained from the freshly placed catheter. Catheter-associated asymptomatic bacteriuria (CA-ASB) is defined as culture growth of $\geq 10^5$ colony forming units (cfu)/mL of uropathogenic bacteria in the absence of symptoms compatible with UTI in a patient with indwelling urethral, indwelling suprapubic, or intermittent catheterization[7].

In some patients with bacteriuria, removal of the catheter suffices to eradicate the infection. To reduce the risk of urinary tract infection (UTI), antibiotic treatment may be considered in patients with asymptomatic bacteriuria that persists 48 hours after removal of a short-term indwelling catheter. A specimen for urine culture should be obtained before initiation of antibiotic therapy, because of the wide spectrum of potential infecting organisms and the increased likelihood of antimicrobial resistance[5]. In patients whose symptoms resolve promptly, 7 days is the recommended duration of antibiotic treatment. In those with a delayed response or with bacteremia, 10-14 days of treatment is recommended. In women older than 65 years who develop a UTI after removal of an indwelling catheter and who have no upper urinary tract symptoms, a 3-day antimicrobial regimen may be considered[5].

Aseptic indwelling catheter insertion, a properly maintained closed-drainage system (with ports in the distal catheter for needle aspiration of urine), and unobstructed urine flow are essential for prevention of UTI. Hand hygiene is obviously of paramount importance in catheter insertion and catheter care. Adequate lubrication during catheter insertion prevents mucosal trauma, and the narrowest catheter appropriate to good drainage (14 or 16F) allows drainage of periurethral secretions[9]. Urinary catheters coated with silver alloy also reduce the risk of infection[10]. An alternative is to use all silicone catheters, which have a hydrophilic coating that decreases tissue irritation and nosocomial UTIs. It is reasonable to use these more expensive catheters in patients who are at highest risk. However, a 2012 study failed to find any advantage in the short-term use of silver alloy-coated and nitrofurantoin-impregnated catheters in reducing symptomatic urinary tract infections[11]. One adult neurological intensive care unit implemented an evidence-based “UTI bundle” focused on the avoidance of catheter insertion, maintenance of sterility, product standardization, and early catheter removal. In a 30-month period, catheter-associated UTIs significantly decreased (from 13.3 to 4.0 infections per 1000 catheter days), with a linear relationship between catheter use rate and catheter-associated UTIs[12].

Several expert and governmental groups have released guidelines or recommendations on the identification, management, and prevention of catheter-associated urinary tract infections (UTIs)[6,7,9,13,14,15]. A comprehensive update has been produced as a collaborative effort by the European Society for Infections in Urology, Urological Association of Asia, the Asian Association of UTI/STD, the Western Pacific Society for Chemotherapy, the Federation of European Societies for Chemotherapy and Infection, and the International Society of Chemotherapy for Infection and Cancer. This text was recently published as “The European and Asian guidelines on management and prevention of catheter-associated urinary tract infections” and is an important reference the
reader is referred to\cite{13}. In 2014, a collaborative panel sponsored by the Society for Healthcare Epidemiology of America (SHEA) released recommendations on the prevention of catheter-associated UTI\cite{15}. All publications highlight the importance of the judicious use of urethral catheters only for appropriate indications, adequate expertise and sterile technique for insertion, continued assessment of the necessity of catheterization, and maintenance of a sterile, continuously closed drainage system that allows unobstructed urine flow, and the avoidance of unnecessary antibiotic use for asymptomatic bacteriuria.

**References:**

Original Article

A Study of Catheter Associated Urinary Tract Infection in Intensive Care Unit of a Tertiary Care Hospital in Kolkata

Dr. Arjun Ray¹, Dr. Jayanta Chakraborty², Dr. Prabuddha Mukherjee³

Abstract:
Urinary tract infections comprise 40% of all institutionally acquired infections worldwide. Out of these, more than 80% are associated with an indwelling catheter. It has been estimated that about 69% of hospital acquired CAUTI may be prevented by implementation of an evidence-based prevention program. Hospital specific data concerning its incidence and attributes are essential to its effective control. A prospective observational study of 50 inpatients in ICU of RKMSP with indwelling catheter & signs & symptoms suggestive of CAUTI was carried out from 5th September 2013 to 22nd February 2014. Total patients admitted in ICU during the same time period was 563 among whom 125 patients were catheterized. 50 of these newly catheterized patients developed signs & symptoms consistent with CAUTI. The aim of this study was to identify the incidence in various age groups & sex distribution of CAUTI in a tertiary care hospital in Kolkata, to find out the common organisms associated with CAUTI and to establish the antibiotic sensitivity pattern of the isolated strains.

Results:
Among these 125 patients with indwelling catheter 50 patients (40%) aged between 20 years to 79 years (mean age 62.96 yrs, SD 15.54) developed CAUTI; major prevalence was among middle aged people i.e. 40-59 yrs (48%) closely followed by elderly population i.e. 60-79 yrs (44%). Females are leading the race (64% for females vs 36% for males). The mean number of days from date of catheterization to onset of first symptoms was 4.12 (SD 1.84). Gram negative bacteria in the form of Escherichia Coli is the major offender (58%) among which only a meager 22% are Betalactam sensitive. Rest are Carbapenem resistant (CRE) (26%) & Extended spectrum Betalactamase (ESBL) producing strains (10%). Overall CRE strains among all isolates are about 38% followed by ESBL producing strains (16%). Fungal infections causing CAUTI is about 10%.

Conclusion:
Widespread isolation of polyantimicrobial resistant nosocomial pathogens is one major area of concern. But still about 36% of overall strains are betalactam sensitive. Overuse of antibiotics, especially for asymptomatic bacteriuria (ASB) may lead to selection of resistant strains & hence should be strictly discouraged. Strict vigilance against indiscriminate insertion of urinary catheter should be our primary goal. Indwelling catheters should be removed as soon as they are no longer required. Routine surveillance of nosocomial infections in the hospital, coupled with the institution of evidence-based antibiotic prescription policy is the unmet need of the day.

Keywords:
Catheter associated urinary tract infection, Extended spectrum Betalactamase, Carbapenem resistant Enterobacteriaceae, Asymptomatic bacteriuria, Health care-associated infection prevention, urinary catheter.

¹Post Graduate Trainee, Dept. of Gen. Medicine, RKMSP, VIMS; ²Prof. & HOD, Dept. of Gen. Medicine, RKMSP, VIMS; ³Asst. Prof., Dept. of Gen. Medicine, RKMSP, VIMS
Introduction:

Urinary tract infections are one of the five most common types of healthcare-associated infection (HAI), accounting for 40 percent of all hospital HAIs[1,2]. Majority of healthcare-associated UTIs are caused by instrumentation of the urinary tract. CAUTI in patients with indwelling urethral, indwelling suprapubic, or intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identified source of infection along with 10^{5} colony forming units (CFU)/mL of = 1 bacterial species in a single catheter urine specimen from a patient with indwelling catheter for >2 calendar days or in a midstream voided urine specimen whose urethral or suprapubic catheter has been removed within the previous 48 hours[3]. Catheter-associated urinary tract infection (CAUTI) has been associated with increased morbidity, mortality, hospital cost, and length of stay. Bacteriuria also leads to unnecessary antimicrobial use, and urinary drainage systems can be reservoirs for multidrug-resistant bacteria and a source of transmission to other patients.

Five risk factors associated with the later development of CAUTI: 1) duration of catheterization, 2) catheter care violations, 3) absence of systemic antibiotics, 4) female gender and 5) older age[4].

The CDC reports that the most frequent pathogens associated with CAUTI in hospitals reporting to NHSN between 2006 and 2007 were Escherichia coli (21.4 percent) and Candida spp (21 percent), followed by Enterococcus spp (14.9 percent), Pseudomonas aeruginosa (10 percent), Klebsiella pneumoniae (7.7 percent), and Enterobacter spp (4.1 percent). A smaller proportion was caused by other gram-negative bacteria and Staphylococcus spp[9].

The purpose of this study was to examine the particular offending strains and to formulate a rigorous antibiotic stewardship so as to cut down the prevalence of multi drug resistant organisms in the near future.

Objectives:

1. To find out the prevalence of CAUTI
2. To identify the incidence in various age groups & sex distribution.
3. To find out the common organisms associated with CAUTI.
4. To establish the antibiotic sensitivity pattern of the isolated strains.

Materials:

Type of Study: Prospective observational study

Sample Population: 563 inpatients in ICU of RKMSP among whom 125 had indwelling catheter. 50 of those with indwelling catheter & signs & symptoms suggestive of CAUTI were surveyed for the final analysis.

Time Period: September 2013 to February 2014
Parameters: 1. Date of catheterization. 2. Onset of first symptoms. 3. Recatheterized or not. 4. Date of initiation of antibiotics

Investigations: Urine specimen for routine examination & microbiologic culture with antibiotic sensitivity pattern.

Methodology:
A prospective observational study among 563 inpatients in ICU of RKMSP was carried out from 5th September 2013 to 22nd February 2014. Ours is a multidisciplinary ICU, with arrangement of each bed in a separate cubicle with nurse patient ratio of 1:3. The profile of patients admitted were perforation peritonitis, pneumonia, cardiac failure, acute myocardial infarction etc. Of them 125 had been on indwelling catheter which was not in situ during time of admission. All catheterized patients with culture positive urine specimens and signs & symptoms suggestive of CAUTI were included in the study. This study categorically excluded patients admitted with catheter in situ at admission. ICU nurses or and physicians inserted urinary catheters using aseptic technique with a 2% chlorhexidine preparation for skin antisepsis. Catheter type used could be Foley’s or suprapubic catheter[4]. CAUTI was diagnosed after placement of catheter for >2 calendar days or within 48 hours after catheter removal. Patients had at least one of the following signs or symptoms like fever (>38.0°C), suprapubic tenderness & costovertebral angle pain or tenderness[6]. And finally a urine culture with no more than two species of organisms, at least one of which is a bacteria of $=10^5$ CFU/ml guided our diagnostic criteria of catheter associated UTI in the ICU setup. Catheter insertion and maintenance were in accordance with CDC guidelines. Urinary catheters were not routinely replaced. The decision to remove a catheter was made solely by the patient’s physician, with catheters kept in place until it is no longer needed or until an adverse event necessitates its removal. Placement of a catheter was considered appropriate when the indication was for close monitoring of urine output in an incontinent patient or in a critically ill patient requiring intensive monitoring during vasopressor infusion[7]. A urine specimen for culture was obtained prior to initiating antimicrobial therapy for presumed CAUTI because of the wide spectrum of potential infecting organisms and the increased likelihood of antimicrobial resistance. Urine specimen collected aseptically for routine examination & culture with antibiotic sensitivity pattern was studied rigorously for final analysis.

Results:
Among 125 inpatients of ICU with an indwelling catheter a total of 50 patients aged between 20 years to 79 years (mean age 62.96 yrs, SD 15.54) satisfied the diagnostic criterion of CAUTI. Almost a whopping 40% prevalence of CAUTI was found out among the catheterized patients; major prevalence was among middle aged people i.e. 40-59 yrs (48%) closely followed by elderly population i.e. 60-79 yrs (44%). Young age group (20-39 yrs) comprising a meager 8% of all cases.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Frequency</th>
<th>Percent</th>
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<tr>
<td>Elderly (60-79 yrs.)</td>
<td>22</td>
<td>44</td>
</tr>
<tr>
<td>Middle age (40-59 yrs.)</td>
<td>24</td>
<td>48</td>
</tr>
<tr>
<td>Young (20 - 30 yrs.)</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 1. Table showing the distribution of CAUTI in different age groups.
Table 2. Bar diagram showing the distribution of CAUTI in different age groups.

Prevalence of CAUTI was much more in women. (64% for females vs 36% for males)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency</th>
<th>Percent</th>
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</thead>
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<tr>
<td>F</td>
<td>32</td>
<td>64</td>
</tr>
<tr>
<td>M</td>
<td>18</td>
<td>36</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100.0</td>
</tr>
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</table>

Table 3. Table showing the sex distribution of CAUTI.

Table 4. Pie Chart showing the sex distribution of CAUTI.

The mean number of days from date of catheterization to onset of first symptoms was 4.19 (SD 1.84); median number of days from date of catheterization to onset of first symptoms being 4 and mode 3.

Gram negative bacteria in the form of E.coli is the major offender (58%) among which only a meager 22% are Beta lactam sensitive. Rest are Carbapenem resistant (CRE) (26%) & Extended spectrum Beta lactamase (ESBL) producing strains (10%). Overall CRE strains among all isolates are about 38% followed by ESBL producing strains (16%). Fungal infections causing CAUTI is about 10%.

Table 5. Graphical representation of E.Coli drug sensitivity pattern.

Extended-spectrum β-lactamases (ESBLs) are a rapidly evolving group of β-lactamases which share the ability to hydrolyze third-generation cephalosporins and aztreonam yet are inhibited by clavulanic acid. Carbapenems are the treatment of choice for serious infections due to ESBL-producing organisms, yet carbapenem-resistant isolates have recently been reported coming under the broad group of Carbapenem resistant Enterobacteriaceae.
**Organisms** | **Frequency** | **Percent**
--- | --- | ---
Acinetobacter Baumannii | 1 | 2
Candida Albicans | 2 | 4
Candida Lusitaniae | 1 | 2
Candida Tropicalis | 2 | 4
Citrobacter Freundii | 1 | 2
E.Coli | 29 | 58
Enterococcus Gallinerum | 2 | 4
Klebsiella Pneumonia | 7 | 14
Proteus Mirabilis | 2 | 4
Pseudomonas Aeruginosa | 3 | 6
**Total** | **50** | **100.0**

**Table 6. Frequency distribution table of organisms isolated in CAUTI.**

**Table 7. Pie Chart showing organisms isolated in CAUTI.**

**Antibiotic Sensitivity Pattern**

Only 36% of overall strains were Beta lactam sensitive; 22% being E.coli that retained sensitivity to beta lactams followed by Klebsiella (8%). Carbapenem resistant organisms accounted for 38% of all isolated organisms, 26% being Carbapenem resistant E.coli, 4% being Pseudomonas and rest being the less frequently isolated organisms like Acinetobacter, Proteus or Klebsiella or Citrobacter. ESBL producing Gram negative organisms accounted for 16% of all isolates; 16% being E.coli.

**Discussion:**

There were four main findings from this study. First of them being the fact that prevalence of CAUTI was a real concerning 40% among the patients with an indwelling catheter not present in situ at the time of admission; maximum (about 48%) being in the age group 40-59 yrs closely followed by the elderly population aged between 60-79 yrs. The reason is that the previous group consisted of people in the reproductive age and...
adults who may have been sexually active. Whereas the following group consisted of critically ill persons on admission, who had undergone surgery or may be patients of neurological case, urological, trauma or a case of acute onset respiratory failure, this agrees with the finding of Lorente et al in 2005.

The microorganism with the highest rate is E.coli with 58%, followed by Klebsiella pneumoniae (14%). This may be because E.coli is the predominant organism in the gut among Enterobacteriaceae, an infection of urinary tract by contaminating the urethra and ascending into the bladder is the most probable explanation of this preponderance (Patrick et al; 1998). Candida albicans isolation may be predominantly from diabetes or immunocompromized patients. This agrees with the study of Raphael et al in 2009. In a study done on the prevalence of urinary catheter related infections in Federal Medical centre, Abeokuta, Nigeria; out of 200 samples examine, 82 (41.10%) yielded growth of bacteria while 118 (59.00%) were negative. The urine of the 82 positive cases yielded E. Coli 29 (35.40%), Klebsiella pneumoniae 17(20.9%).

Pseudomonas aeruginosa 10 (15.5%), S. aureus 13 (12.1%), Proteus mirabilis (9.75%) and C. albicans (6.0%). The age group that was most affected was 26-35 years (32.0%), followed by 36-45 years (20.70%), 46-55 (9.80%), 66-75 (8.50%) and 86-95 (8.50%) while age group 56-65 (7.31%) and 76-85 (7.31%) had least. Females were more prone to the urinary catheter related infection. In this study with females comprising of 64% & with male value of 36% this is in disagreement with Lorente et al in 2005. The reason may be due to shorter urethral and wider female urethra appearing to be less efficient in preventing access of the bacteria to the bladder while less number in men may be due to longer urethra and bactericidal activities of the prostatic fluid. Female are more vulnerable to catheter infections. The antibiotic susceptibility testing revealed high sensitivity of E. Coli to Augmentin (41.4%), Klebsiella pneumonia to Ofloxacin (52.90%), Proteus mirabilis (30.00%) & Pseudomonas aeruginosa to Ofloxacin (21.42%) and S. aureus to both Ofloxacin and Gentamycin.

In a three-year retrospective study on nosocomial complicated urinary tract infections, a rural based referral hospital study conducted by A. RAMANI et al conducted in 891 patients, eighty-eight per cent of the patients had complicated urinary tract infections with predominantly nosocomial organisms such as Klebsiella as opposed to the normally more common uncomplicated infection with E. coli. The reasons for this were probably the delay in referral, resulting in late correction of the underlying structural causes of the infections. In our study, Gram negative bacteria in the form of E Coli is the major offender (58%) among which only a meager 22% are Betalactam sensitive. Rest are Carbapenem resistant (CRE (26%) & Extended spectrum Betalactamase (ESBL) producing strains (10%). Overall CRE strains among all isolates are about 38% followed by ESBL producing strains (16%). Fungal infections causing CAUTI is about 10%. However ours is an urban hospital and this study was conducted in ICU settings with round the clock monitoring of patients status and complications.

In the above mentioned study, microbial sensitivity tests revealed that most of the commonly used antibiotics were ineffective in the majority of patients. The efficacy of ampicillin was found to be as low as 3%. Similar
Discouraging patterns were found with other commonly used antibiotics such as co-trimoxazole (21%), sulphadiazine (1%) and doxycycline (9%). The emergence of resistant isolates in the form of CRE & ESBL strains were associated with longer duration of ICU stay, rampant use of antibiotics without keeping into account the antibiotic sensitivity pattern of the cultured strains, unnecessary practice of catheterization and prior antibiotic usage due to other comorbidities. In our hospital however, still 36% isolates were beta lactam sensitive probably resulting from reasonable antibiotic usage practices. Hence a prudent antibiotic stewardship programme developed specifically for this hospital in conjunction with the Department of Microbiology might aid in the prevention of emergence of further “bad bugs”.

References:


A Study on The Etiology of Ascites & Incidence of Spontaneous Bacterial Peritonitis in a Tertiary Care Hospital in Kolkata

Dr. Sunetra Mondal¹, Dr. Jayanta Chakraborty², Dr. Prabuddha Mukherjee³

Abstract:
Ascites could develop due to a host of etiologies like portal hypertension due to chronic liver disease, nephritic syndrome, congestive cardiac failure, malignancies and many other causes. Ascitic fluid study specially SAAG helps in determination of cause of ascites. Spontaneous bacterial peritonitis and other related ascitic fluid infection are dreadful complications that develop particularly in CLD patients which might be prevented by prophylaxis and early detection in high risk patients. A prospective observational study on patients admitted with ascites in RKMSP, Dept of Medicine, from July to December 2013 was done with the objectives to study the etiology of ascites in these patients, to study the incidence of spontaneous bacterial peritonitis among them, to calculate the Child pugh’s score among the patients with ascites due to chronic liver disease and try to find a correlation between Child pugh’s score and the occurrence of SBP.

Results:
35 patients were admitted with ascites in the wards of Medicine, RKMSP during July to Dec 2013; 21 of them being males (60%) and remaining 14 (40%) females. The mean age of the study population was 57.48; SD 11.75. Chronic liver disease (60%) followed by malignant ascites (21%) accounted for most of the cases. Tubercular, nephrotic syndrome and cardiac cause accounted for 5.71% each. 8 out of 35 (22.84%) of the patients developed Spontaneous bacterial peritonitis; 5 cases (62.5%) of the SBP cases being in CLD patients. Out of these 5 patients, 3 patients (60%) were in child pugh grade C and 2 (40%) in grade B.

Conclusion:
Chronic liver disease is the commonest etiology of ascites followed by malignancy. Other common causes could be tubercular ascites, nephrotic syndrome and others. SBP was most common in ascites due to Chronic liver disease, also common in nephrotic syndrome. Ascitic fluid infection in the form of Spontaneous bacterial peritonitis and Culture Negative Neutrocytic Ascites was more in CLD patients with Child Pugh grade C followed by CP grade B.

Keywords:
Ascites, Chronic liver disease, Spontaneous bacterial peritonitis, Child Pugh score.

Introduction:
Ascites referring to the fluid accumulation within the peritoneal cavity could be due to a host of pathologic causes affecting any of the systems involved in maintenance of fluid balance or due to excess fluid secretion from the peritoneal lining cells. Determination of the cause of ascites is based on the results of the history, physical examination and ascitic fluid analysis. WBC count in uncomplicated ascites is usually <500 cells in the absence of overt diuresis. However the cut off point for PMN values of 250 remain

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reliable even after diuresis. Serum Ascitic Albumen gradient has been proved to categorize ascites better than other parameters. High SAAG Ascites is usually due to portal hypertension due to cirrhosis or cardiac causes.

<table>
<thead>
<tr>
<th>SAAG&gt;=1.1</th>
<th>SAAG&lt;1.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCITIC PROTEIN &gt;2.5</td>
<td></td>
</tr>
<tr>
<td>* CCF/CONSTRICTIVE PERICARDITIS</td>
<td></td>
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<tr>
<td>* IVC OBSTRUCTION</td>
<td></td>
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<tr>
<td>* EARLY BUDD CHIARI</td>
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</tr>
<tr>
<td>* MYXEDEMA</td>
<td></td>
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<tr>
<td>ASCITIC PROTEIN 2.5</td>
<td></td>
</tr>
<tr>
<td>* CIRRHOSIS OF LIVER</td>
<td></td>
</tr>
<tr>
<td>* MASSIVE LIVER METS</td>
<td></td>
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<tr>
<td>* LATE BUDD CHIARI</td>
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</tbody>
</table>

BILIARY ASCITES
NEPHROTIC SYNDROME
PANCREATIC ASCITES
PERITONEAL CARCINOMATOSIS TUBERCULAR
POST OP LYMPH LEAK BOWEL INFARCTION

Ascitic fluid infection can be classified into five broad categories based on culture, PMN count and presence or absence of surgical sources of infection.

1. **Spontaneous Ascitic Fluid Infection:**
   - SBP (Spontaneous Bacterial Peritonitis)
   - CNNA (Culture Negative Neutrocytic Ascites)
   - MNBA (Monomicrobial Bacterascites)

2. **Surgical:**
   Secondary Bacterial Peritonitis
   Polymicrobial bacterascitis (d/t intestinal perforation by paracentesis needle)

SBP = Positive AF culture for a single organism; PMN>250; no intra abdominal surgical source of infection. Though many patients with SBP might have a separate focus of infection like UTI or pneumonia etc they will still be appropriately called a “spontaneous” bacterial infection unless the focus requires surgical intervention.

MNBA = Positive AF culture for a single organism; PMN <250; no intra abdominal surgical source of infection; previously known as asymptomatic bacterascitis, a misnomer.

CNNA = Ascitic fluid shows no growth of bacteria; AF PMN>250 in absence of other causes for the same (like hemorrhage or peritoneal carcinomatoses); mostly due to insensitive culture methods.

Polymicrobial Bacterascites = Multiple organisms are seen on Gram stain or cultured from ascitic fluid; PMN<250. Occurs after needle perforation of distended viscus by paracentesis needle.

Spontaneous forms of ascitic fluid infection are the result of overgrowth of a specific organism in the intestine, “translocation” of the microbe from intestine to mesenteric lymph nodes and resulting spontaneous bacteremia and subsequent colonization of ascitic fluid. The endogenous antimicrobial (opsonic) activity of human ascitic fluid correlates directly with protein concentration of the fluid. Patients with good opsonic activity develop sterile non neutrocytic ascites, moderate opsonic activity develop CNNA, and AF with low protein have poor opsonic activity and predisposed to develop SBP. GI bleeding further increases the risk by shock mediated increase in translocation of bacteria from intestinal to extraintestinal sites.

In the past 48 to 95% of patients with spontaneous AF infection died during hospitalisation despite antibiotic treatment. However earlier detection of SBP has lowered the incidence significantly. This could be by paracentesis at admission and prudent repeat
paracentesis if any suspicion of SBP arises. Prophylactic antibiotic administration may help to prevent SBP in patients with high risk.

**Objectives:**

1. To study the etiology of ascites in patients admitted in the Dept of Medicine in RKMS from July to December 2013.

2. To study the incidence of Spontaneous bacterial peritonitis among these patients with ascites.

3. To calculate the Child Pugh’s score among the patients with ascites due to chronic liver disease and try to find a correlation between Child Pugh’s score and the occurrence of SBP.

**Methods:**

**Study Type:** Prospective Observational study.

**Study Period:** July 2013 to December 2013.

**Study Population:** Patients admitted with ascites in the Medicine wards of Ramkrishna Mission Seva Pratisthan, Kolkata.

**Parameters to be Studied:** Age, sex, detailed history and clinical examination with special reference to points favoring the etiological diagnosis of ascites and severity of chronic liver disease. Relevant investigations were done.

**Investigations:**

- Hb, TC, DC, Platelet, CRP.
- Urea/Creatinine, Electrolytes, LFT, PT/INR, lipids.
- Urine R/E, 24 hr urinary protein.
- Ascitic Fluid study cell type with Gram and ZN stain, cell count, Culture.
- Ascitic fluid albumen, SAAG, protein, sugar.
- Echocardiography (if indicated).

**Methodology:**

Patients admitted in Dept of Medicine, RKMS with ascites were enquired for a detailed history which might point towards etiology. Ascites was either demonstrable clinically or diagnosed by USG. History included their age, time since first detection of ascites, whether first or recurrent episode, history of jaundice, pedal swelling or periorbital puffiness and their temporal relation to ascites, history of oliguria, palpitation; history suggestive of malignancy anywhere. For patients suspected of having chronic liver disease, a history suggestive of any bleeding manifestation including hematemesis/melena, history suggestive of hepatic encephalopathy and its grade were noted to aid in the calculation of Child Pugh’s score was noted. History of fever and abdominal pain suggesting the possibility of spontaneous bacterial peritonitis was noted. Patients with suspected secondary surgical cause of peritonitis were excluded from the study. Meticulous general and systemic clinical examination was done. Pallor, Icterus, pedal edema, lymphadenopathy, the degree of ascites, hepatosplenomegaly, abdominal tenderness and a detailed cardiovascular examination were given special emphasis. The neuropsychiatric status was evaluated and encephalopathy, if any was graded according to West Haven Criteria. Relevant Investigations were done. Complete Blood count was done to rule out pancytopenia due to hypersplenism d/t CLD, pallor or leucocyte changes due to malignancy, leukocytosis sue to SBP. LFT was done to suggest hepatic cause, seum albumin to calculate SAAG, serum biliubin and PT/INR to calculate Child Pugh’s score in patients with chronic liver disease. Urea/Creatinine; urine R/E and 24 hrs urinary protein (for those showing presence
albumin in urine) was noted to help diagnose nephrotic syndrome. ECG and ECHO cardiography were done for those in whom cardiac cause was suspected. Lipid profile was done for nephrotic syndrome as well as a cardiovascular risk factor. Raised CRP served as a non specific inflammatory marker suggesting the presence of SBP in those without leukocytosis.

Diagnostic paracentesis was done aseptically with proper precautions in all the subjects and ascitic fluid protein, albumen (to calculate SAAG), LDH, sugar, cell count, cell type, presence of malignant cells were noted. A cut-off value of 1.1 for SAAG was used to define high and low SAAG ascites.

For Ascitic fluid Culture study bedside inoculation into blood culture bottles (= 10 mL) were done and simultaneous blood samples were also cultured to rule out septicemia.

Conditions related to ascites were defined as follows:

1. **Bacterascites** for positive ascitic fluid culture, ascites PMN < 250/mm³ and no evidence of local or systemic infection.

2. **Culture-negative neutrocytic ascites (CNNA)** was diagnosed when the ascitic fluid culture did not grow pathogenic bacteria, but the ascitic fluid neutrophil count was at least 250/mm³.

3. **Secondary peritonitis**: suspected when any of the following:
   - Two or more organisms isolated (particularly anaerobes or fungi).
   - At least 2 of the following findings in ascitic fluid: glucose < 50 mg/dL; protein > 10 g/L; lactate dehydrogenase > normal serum levels.

   These subjects were excluded from the study.

The age, sex, history of recurrence of ascites and ascitic fluid parameters including SAAG, protein, cell count, type and culture growth of organisms and the final etiologic diagnosis reached on the basis of clinical and laboratory values were tabulated and the prevalence of each etiology studied. The incidence of SBP was calculated and the etiology of the underlying ascites noted. For patients with chronic liver disease, Child Pugh’s score was calculated and a correlation was tried to be established between the occurrence of SBP and the Child Pugh’s score of the patient.

**Results:**

In the time period between July to December 2013, 35 patients admitted with ascites in the wards of Medicine, RKMSP; 21 of them being males (60%) and remaining 14 (40%) females. 21 (60%) of them had a history of recurrence of ascites requiring hospital admission before this episode.

The mean age of the study population was 57.48; SD 11.75. The age distribution table of the population is as follows:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;=40</td>
<td>2</td>
<td>5.71%</td>
</tr>
<tr>
<td>41-50</td>
<td>8</td>
<td>22.84%</td>
</tr>
<tr>
<td>51-60</td>
<td>12</td>
<td>34.26%</td>
</tr>
<tr>
<td>61-70</td>
<td>11</td>
<td>31.42%</td>
</tr>
<tr>
<td>&gt;70</td>
<td>2</td>
<td>5.71%</td>
</tr>
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</table>

The ascitic fluid parameters of the study population were tabulated and statistically analysed. Mean ascitic Fluid Albumen was 1.58, SD 0.62. The mean SAAG was 2.1, SD 0.43. Nine of the 35 patients (25.71%) had low SAAG.
ascites defines as SAAG <1.1. Remaining 26 patients (74.3%) had SAAG values >=1.1. 7 out of the 35 patients (20%) showed the presence of malignant cells on PAP staining of their ascitic fluids. The mean ascitic fluid cell count was 206.29, SD 139. None of the fluid samples showed the presence of organisms identifiable by Gram/ZN staining. One sample showed the growth of Mycobacterium tuberculosis when inoculated in BACTEC culture for M.TB.

The final etiological diagnosis established for these 35 patients, based on clinical and Ascitic fluid analysis are as follows:

Spontaneous bacterial peritonitis was found in 8 out of the 35 patients (22.84% incidence). 5 out of these 8 (62.5%) developed in patients where Chronic liver disease was the cause of the underlying ascites. 2 cases (25%) developed in patients with nephrotic syndrome and 1 case of SBP (12.5%) developed in malignant ascites.

The 21 patients with ascites due to chronic liver disease were considered for calculation of Child pugh’s score. The age distribution of patients with ascites due to CLD is tabulated as follows:

<table>
<thead>
<tr>
<th>Child Pugh's grade</th>
<th>CLD</th>
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<tbody>
<tr>
<td>&lt;=50</td>
<td>4</td>
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<tr>
<td>51-60</td>
<td>8</td>
</tr>
<tr>
<td>61-70</td>
<td>8</td>
</tr>
<tr>
<td>&gt;70</td>
<td>1</td>
</tr>
</tbody>
</table>

The mean bilirubin for these 21 patients was 2 (SD 0.57); mean INR  1.74 (SD 0.39) and mean serum albumen 1.5 (SD 0.39). The Child Pugh’s score and grade for these patients were calculated and the distribution in different Child Pughs grade is as follows:

<table>
<thead>
<tr>
<th>Child Pugh's grade</th>
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<tbody>
<tr>
<td>A</td>
<td>2</td>
</tr>
<tr>
<td>B</td>
<td>12</td>
</tr>
<tr>
<td>C</td>
<td>7</td>
</tr>
</tbody>
</table>

As discussed earlier, 5 out of the 8 patients with SBP had an underlying CLD as the cause of ascites. 4 patients with CLD developed CNNA (Culture negative neutrocytic acites). The incidence of SBP and CNNA in different Child pughs grades is tabulated as follows:
Ascitic fluid from 7 out of the 8 patients with SBP showed the growth of E. coli on culture. Fluid from one patient showed the growth of Clostridium freundii and the underlying cause was malignant ascites. One patient with bacteraemic ascites showed K. pneumonia growth.

**Discussion:**
Several studies have shown that ascites occurring in the setting of portal hypertension is the most common cause, around 85% due to cirrhosis, due to vasodilation and renal salt and water retention due to RAAS activation. Other causes of portal hypertension could be malignancy induced portal lymph node obstruction or portal vein thrombosis. Remaining could be due to cardiac causes like congestive cardiac failure or constrictive pericarditis or renal causes like nephrotic syndrome. Peritoneal carcinomatosis or infection by Tuberculosis, Chlamydia produce excess proteinaceous peritoneal secretion.

In this study, prevalence of different etiologies of ascites were Chronic liver disease (60%) followed by malignancy, TB and others.
The prevalence of SBP in hospitalized patients with cirrhosis and ascites is between 10% and 30% found by most studies from the west; Tandon P et al, Rimola A et al, Almdal TP et al and Pinzello G et al. The prevalence of SBP in our study was found to be 22.8%. The prevalence of CNNA in this study was also found to be high at 11.42%. This might be due to the late presentation of the patients to our health facility. The higher prevalence of CNNA could be due to lesser detection sensitivity of culture studies in this hospital specially anaerobic culture methods.

87.5% of the cases of SBP showed the growth of aerobic Gram-negative bacilli; with Escherichia coli being the most common. There have been few large scale studies relating Child Pugh's score with the occurrence of Spontaneous Bacterial Peritonitis. In a study conducted in BJMC Ahmedabad published in Jan 2013, of 253 CLD patients with SBP; 78% had Child Pugh's >=10. Similar results were obtained in a study by Kennari et al.

In our study, 60% were in stage C and 40% in stage B. For CNNA, these ratios were 50% in stage B and 50% in stage C.

We haven’t repeated paracentesis for patients with recurrent ascites once the etiology has been established for the costs as well as the risk of precipitating encephalopathy or secondary polymicrobial bacteraemic. However a prudent decision for diagnostic paracentesis must be undertaken for all patients at high risk of developing SBP as early as possible once even subtle suggestive signs develop including abdominal pain, fever, change in mental status,
renal failure, acidosis, peripheral leucocytosis or GI bleeding develops. Survival is almost nil in SBP after creatinine has risen to >4 or shock develops. To maximize survival it is important that paracentesis be performed in all patients with ascites at the time of hospitalisation so that infection can be detected and treated promptly. The first dose of antibiotic should be given within 90-120 sec.

Also these patients with high risk of developing this dangerous complication should be offered antibiotic prophylaxis for the prevention of SBP. Prophylactic antibiotics like norfloxacin and Ceftiaxone in different regimens have already been approved for patients with GI bleeding, low protein ascitic fluid or h/o prior SBP. However other risk factors need to be identified as predictive marker of SBP and initiation of prophylactic antibiotic therapy in them must be instituted.

References:
Abstract:

Introduction:

Increased level of serum homocysteine has been found to be responsible for macro and microvascular complications in type 2 diabetes mellitus (T2DM). The present study has been undertaken to observe the serum homocysteine status of the type 2 diabetics and the relationship between the glycemic status and serum homocysteine level, as well as to find out prevalence of hyperhomocysteinemia in Indian type 2 diabetics.

Methods:

The serum homocysteine level of 50 consecutive type 2 diabetic patients attending first time in a diabetes clinic, Kolkata were measured along with other parameters and the data obtained was analyzed.

Results:

Mean FPG was 130.30±6.13 mg/dL, mean PPPG was 191.76±10.99 mg/dL, mean HbA1c was 8.2±2.1 mg/dL, mean BMI was 25.29±3.88 kg/m² and the mean serum homocysteine level was 15.12±6.68, when all 50 subjects taken together. Considering the normal range for homocysteine as per laboratory standard (15 IU/l), the value could be considered as highish normal. Further, 34% of the patients showed high value i.e. hyperhomocysteinemia, 50% showed highish normal and only 16% showed low normal value. Further, the fasting as well as the post prandial plasma glucose (PPPG) showed inverse relationship with the serum homocysteine level though statistically insignificant (p > 0.5)

Conclusion:

Serum homocysteine level was found to be raised in 34% of type 2 diabetic patients which indicates scope for intervention. But the glycemic status was negatively related to the homocysteine level though the relationship was not statistically significant, may be due to the small sample size. However, larger population study, which is undergoing presently, is needed to confirm.

Introduction:

Homocysteine is a homologue of the amino acid cysteine, differing by an additional methylene (-CH2-) group. It is biosynthesized from methionine by the removal of its terminal methyl group and can be recycled into methionine or converted into cysteine with the help of B-vitamins. Methionine as such do not have any metabolic functions but homocysteine has been associated with extracellular matrix changes. Numerous studies have pointed towards an association of type 2 diabetes mellitus (T2DM) with elevated homocysteine levels.[1] Acute elevations in circulating homocysteine levels have been found to impair endothelial function in coronary microcirculation in normal subjects.[2] More importantly, several studies have also reported increased levels of homocysteine in T2D patients with microangiopathy, nephropathy and proliferative diabetic retinopathy.[3,4] However, it is yet to be conceived how hyper

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homocysteinemia increases the risk of death in type 2 diabetic patients.\cite{5,6} Though it can be stated that T2DM individuals with chronic elevated levels of homocysteine are at greater increased risk of multiple macrovascular and microvascular complications.

By keeping the above information in mind, the objective of the present study was to investigate the serum homocysteine status of the type 2 diabetics and relationship between the glycemic status and serum homocysteine level, as well as to find out prevalence of hyperhomocysteinemia in Indian type 2 diabetics.

**Materials and Methods:**

This observational study was conducted in the diabetes clinic of a multispeciality hospital in Kolkata, India. Diabetes was diagnosed according to ADA criteria.

After screening, a total of 50 T2DM patients attending the diabetes clinic were included in the study. Patients with a genetic disorder associated with elevated homocysteine levels or on medications known to increase the serum level of homocysteine, like anticonvulsants, theophyline, levodopa, methotrexate etc., malignancy, disease of ovary and pancreas, severe psoriasis, CHF or any major invalidating disease and deficiency disorders like anaemia, hypothyroidism, systemic lupus erythematosus (SLE), anorexia nervosa, organ transplantation, severe skeletal muscle damage or trauma, the patients already on folic acid, pyridoxine and vitamin B12 therapy etc. were excluded from the study.

All patients with diabetes mellitus were evaluated for plasma homocysteine level in association with the glycaemic parameters like fasting plasma glucose (FPG), post prandial plasma glucose (PPG) and glycosylated haemoglobin (HbA1c). The detailed history was taken and relevant clinical examination was performed.

**Results:**

Mean fasting plasma glucose (FPG) was 130.30±6.13 (SD), mean post prandial plasma glucose (PPG) was 191.76±10.99 (SD), mean HbA1c was 8.2±2.1 (SD), mean body mass Index (BMI) was 25.29±3.88 (SD) and the mean serum homocysteine level was found as 15.12±6.68 µg/mL (SD), when all 50 subjects taken together. Considering the normal range for homocysteine as per laboratory standard (16 iu/l), the value could be considered as highish normal. When the values are separated in three groups 34% of the patients showed high value, i.e. hyperhomocysteinemia, 50% showed highish normal and only 16% showed low normal value. Further, the fasting as well as post prandial glucose showed inverse relationship with the serum homocysteine level though statistically insignificant (p>0.5). Which may be related to study design as homocysteine level were measured in a fairly controlled diabetic cohort.

**Discussion:**

Plasma homocysteine were found to be elevated in T2DM and also in pre-diabetes. In the present study, 34% of the patients showed hyperhomocysteinemia and 50% showed highish normal. The prevalence of hyperhomocysteinaemia has been estimated to be 5 per cent in the general population, and 13 - 47 among patients with symptomatic atherosclerotic vascular disease.\cite{8}

In our study, we found the prevalence of hyperhomocysteinaemia to be 34% which is consistent with the previous findings. In our study, the mean plasma Homocysteine level found as 15.12± 6.68 µg/mL (SD) which is
much higher than earlier Indian studies which reported a mean Homocysteine level of 2.69 µg/mL in diabetic patients.[1]

Subjects with elevated Homocysteine are at increased risk of atherothrombotic events. It has been proposed that Homocysteine induced endothelial injury exposes the sub-endothelial matrix leading to platelet activation by various mechanisms like impaired coagulant function, production of reactive oxygen species viz. superoxide and hydrogen peroxide resulting due to auto-oxidation of Homocysteine.[7]

Homocysteine also found to enhance the coagulability by reducing protein C activation, inducing inhibition of antithrombin III, inhibiting the synthesis of anticoagulant heparin sulphate, suppressing thrombo-modulin.

Previous studies have reported elevated Homocysteine levels in diabetic patients with co-morbidities like hypertension, albuminuria independent of other determinants.[9,10] Several studies have provided additional evidence that hyperhomocysteinaemia is an important risk factor for developing vascular diseases including stroke, independent of long recognised factors such as hyperlipidaemia, hypertension, diabetes mellitus, and smoking[11,12] as well as re-stenosis after coronary angioplasty[13,14] Hoogeveen and colleagues have pointed on increased mortality due to CVD in the population of diabetic patients with high Hcy levels in the prospective Hoorn study.[15] Meigs et al. have also found that hyperhomocysteinemia is an independent risk factor of CVD incidence in diabetic patients.[16] Hence, Homocysteine may be considered to act like an mediator through which various risk factors may exert their deleterious effect.

So hyperhomocysteinaemia could serve as another important marker of poor diabetic control and developing complications. Thus, diagnostic measures for Homocysteine in diabetes might be warranted and therapy for lowering raised homocysteine may be administered to those having hyperhomocysteinaemia.

References:


Study of Arsenic Exposure in Oral Carcinoma

Ms. Pritha Pal¹, Dr. Ranjan Raychowdhury², Dr. Ajanta Halder³

Abstract:

Background:
This ongoing study examines any possible correlation of arsenic toxicity with the development of oral malignancy in the patients of West Bengal. Since it is an established fact that arsenic toxicity contributes to the skin cancer and lung cancer but much work has not yet been done in the field of oral cancer, we have attempted the study on the people of West Bengal with oral carcinoma because this state has proven out to be an arsenic prone state in India.

Methodology:
Here we have considered 50 patients with both the premalignant as well as malignant oral lesions, attending our hospital. Their details along with full address were taken down on a questionnaire. The data related to the arsenic affected blocks of different districts of West Bengal were collected from the literature and analyzed with the data related to the number of patients obtained from our study.

Results:
Out of 50 patients, 46 have come from the highly arsenic affected districts of West Bengal and 4 came from the unaffected districts. No patients came from the mildly affected districts. The division of these three groups of districts has been obtained from the literature.

Conclusion:
We can conclude that arsenic toxicity may have a relation with the development of the premalignant and malignant oral lesions in the patients of West Bengal, since maximum number of patients is covered from the highly arsenic affected areas. This can be further confirmed by arsenic estimation of the concerned patients.

Keywords:
Arsenic Toxicity, Oral Cancer.

Introduction:
Oral cancer is known to be one of the most prevalent cancers worldwide. In India, the age standardized incidence rate of oral cancer is 12.6 per 100,000 populations. It is more prevalent in males than in females. Incidence rates for oral cancer vary in men from 1 to 10 cases per 100,000 populations in many countries. It is estimated that 43% of the total cancer deaths are accounted to the use of patent risk factors like alcohol intake, use of tobacco, unhealthy diet and various other infections like that of HPV infection. Heavy metals like chromium, lead, arsenic, nickel etc. in soils may exert their effects on human health through the food grown on them, which may put people under a higher risk of cancer development, if the metal is proved to be a carcinogen. Many countries like Taiwan (mainly Central and Eastern parts) have alarming levels of oral cancer incidence, many cases accounting to the arsenic exposure. Since West Bengal has been known to be an arsenic prone state, we have chosen this zone in our study to find out a possible correlation between the

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arsenic toxicity and the development of oral malignancy.

**Materials and Methods:**

After obtaining the approval of the Ethics Committee of our institute, the study was carried out. Fifty consecutive patients with premalignant and malignant oral lesions who attended our hospital were chosen for this retrospective study. A standard questionnaire was administered to obtain their epidemiological data. Data relating to arsenic contamination in 129 blocks of 8 districts of West Bengal and 100 wards of Kolkata were obtained from the paper: Status of groundwater arsenic contamination in the state of West Bengal, India: A 20-year study report, D. Chakraborti et al., Mol. Nutr. Food Res. 2009, 53, 542 – 551. Both the data sets relating to the geographic distribution of the patients and the arsenic affected districts were finally analyzed to find out any possible correlation between them.

**Results:**

It has been observed that in the literature, the state of West Bengal has been divided into three groups of arsenic affected areas, based on the maximum permissible limit of arsenic concentration in groundwater (50µg/L; recommended by World Health Organization) namely, highly affected (Out of 149 blocks in 8 districts and 100 wards of Kolkata, 107 blocks and 30 wards are affected), mildly affected (Out of 29 blocks in 5 districts, 4 blocks are affected) and unaffected (Out of 63 blocks in 5 districts, none is affected). In our study, 50 patients were chosen who came from different districts of West Bengal. Out of them, 46 came from the highly arsenic affected areas and 4 came from the unaffected areas. None came from the mildly affected areas. So, this group has been opted out from our study. The geographic distribution of the patients is given in the Table 1.

<table>
<thead>
<tr>
<th>Districts</th>
<th>No. of Patients (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolkata</td>
<td>23</td>
</tr>
<tr>
<td>North 24 Parganas</td>
<td>8</td>
</tr>
<tr>
<td>South 24 Parganas</td>
<td>7</td>
</tr>
<tr>
<td>Howrah</td>
<td>6</td>
</tr>
<tr>
<td>Murshidabad</td>
<td>1</td>
</tr>
<tr>
<td>Nadia</td>
<td>1</td>
</tr>
<tr>
<td>Purulia</td>
<td>1</td>
</tr>
<tr>
<td>Midnapur (East)</td>
<td>2</td>
</tr>
<tr>
<td>Midnapur (West)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 1: Geographic Distribution of Patients**

The comparison of the two data relating to the highly arsenic affected districts of West Bengal and the geographic distribution of the patients coming from those districts can be made by the maps of West Bengal in Figure 1 and Figure 2. The tabular comparison is shown through Table 2 and Table 3.
Figure 1: % of Arsenic Affected Blocks.

<table>
<thead>
<tr>
<th>Districts</th>
<th>% of Blocks Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadia</td>
<td>100</td>
</tr>
<tr>
<td>North 24 Parganas</td>
<td>95.4</td>
</tr>
<tr>
<td>Murshidabad</td>
<td>92.3</td>
</tr>
<tr>
<td>South 24 Parganas</td>
<td>64.7</td>
</tr>
<tr>
<td>Howrah</td>
<td>58.3</td>
</tr>
<tr>
<td>Kolkata</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 2: % of Arsenic Affected Blocks of Highly Affected Districts of West Bengal

The comparison of the two data relating to the arsenic unaffected districts of West Bengal and the geographic distribution of the patients coming from those districts can be made by the maps of West Bengal in Figure 3 and Figure 4. The tabular comparison is shown through Table 4 and Table 5.

Figure 2: % of patients.

<table>
<thead>
<tr>
<th>Districts</th>
<th>% of Blocks Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kolkata</td>
<td>46</td>
</tr>
<tr>
<td>North 24 Parganas</td>
<td>16</td>
</tr>
<tr>
<td>South 24 Parganas</td>
<td>14</td>
</tr>
<tr>
<td>Howrah</td>
<td>12</td>
</tr>
<tr>
<td>Nadia</td>
<td>2</td>
</tr>
<tr>
<td>Murshidabad</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3: % of Patients Coming from Highly Affected Districts of West Bengal

The comparison of the two data relating to the arsenic unaffected districts of West Bengal and the geographic distribution of the patients coming from those districts can be made by the maps of West Bengal in Figure 3 and Figure 4. The tabular comparison is shown through Table 4 and Table 5.
Table 4: % of Arsenic Unaffected Blocks of Unaffected Districts of West Bengal

<table>
<thead>
<tr>
<th>Districts</th>
<th>% of Blocks Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulia</td>
<td>0</td>
</tr>
<tr>
<td>Midnapur (East)</td>
<td>0</td>
</tr>
<tr>
<td>Midnapur (West)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 5: % of Patients Coming from Unaffected Districts of West Bengal

<table>
<thead>
<tr>
<th>Districts</th>
<th>% of Blocks Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulia</td>
<td>2</td>
</tr>
<tr>
<td>Midnapur (East)</td>
<td>4</td>
</tr>
<tr>
<td>Midnapur (West)</td>
<td>2</td>
</tr>
</tbody>
</table>

Discussion:

Elevated concentrations of heavy metals in the soil reflect somewhat the levels of exposure to the human body, which may promote cancer development in local residents. Such findings of heavy metal toxicity have proven out to be a carcinogen in many places of Taiwan. Higher incidences of micronuclei (MN), chromosomal aberrations (CA), sister chromatid exchanges (SCE) and aneuploidy have also been reported from the human populations exposed to arsenic through drinking water in various countries. So,
arsenic has become an alarming risk factor for the development of oral malignancy. Potential involvement of the mutated genes of Glutathione S-transferases (GSTs) enzymes, caused by arsenic toxicity, comes out to develop into carcinoma, which can be easily analyzed by CA and MN assays. Since arsenic toxicity is a proven factor of skin cancer, lung cancer and bladder cancer and this metal is highly prevalent in the groundwater of West Bengal at a concentration above 50µg/L (recommended by World Health Organization), it is an alarming time to focus on its effect over the occurrence of oral malignancy, the latter being on an increasing note in this zone.

**Conclusion:**
In the present investigation, maximum number of patients with premalignant and malignant oral lesions has come up from the highly arsenic affected districts of West Bengal (as per literature). So, we can conclude that there may be a possible correlation between the arsenic toxicity and the development of oral cancer in this state. However, a very few percentage of patients have also come up from the unaffected district, which may account to the effect of the established risk factors of oral malignancy. It is also definitive that a larger sample size and proper evaluation of arsenic exposure by chemical assay are required for a much proper conclusion in this field.

**Acknowledgement:**
We are grateful to Swami Satyadevananda, Secretary of Ramakrishna Mission Seva Pratishthan to kindly allow us to conduct the study in this institution. We are also thankful to DST Inspire Fellowship, New Delhi for giving the financial assistance to carry out the study.

**References:**
5. M Patra, A Halder, N Bhowmick, M De; Use of Black Tea in Modulating Clastogenic Effects of Arsenic in Mice In Vivo, West Bengal, India; Journal of Environmental Pathology, Toxicology and Oncology 2005; 24(3)201-210.
8. D. Das, G. Samanta, B. Kumar Mandal, T. Roy Chowdhury, C Ranjan Chanda, P. Pratim Chowdhury, G. Kumar Basu and D. Chakraborti; Arsenic in ground water in six districts of West Bengal, India; Environmental Geochemistry and Health 1996, 18, 5-15 (0269-4042).
Role of Environmental Pollution on Genetic Diseases Especially Down Syndrome

Ms. Gargi Podder¹, Dr. Madhusnata De²

Abstract:
There are many different causes of mental retardation, both biological and environmental. In about 5% of cases, retardation is transmitted genetically, usually through chromosomal abnormalities, such as or fragile X syndrome. Down syndrome occurs when there is an extra chromosome in the 21st pair of chromosomes (known as trisomy 21). People with Down syndrome have 47 chromosomes instead of the normal 46. The disorder occurs in one out of every 600-700 births worldwide. The symptoms of mental retardation are usually evident by a child's first or second year. In the case of Down syndrome, which involves distinctive physical characteristics, a diagnosis can usually be made shortly after birth. Mentally retarded children lag behind their peers in developmental milestones such as sitting up, smiling, walking, and talking. They often demonstrate lower than normal levels of interest in their and responsiveness to others, and they are slower than other children in reacting to visual or auditory stimulation. Radiation, chemicals and other hazards in the environment can endanger the fetus. Chromosomal abnormalities are higher among the offspring of fathers exposed to high levels of radiation in their occupations. Environmental pollutants and toxic wastes are also sources of danger to unborn children. Among the dangerous pollutants and wastes are carbon monoxide, arsenic, mercury and lead. By the time a child reaches the age of two or three, retardation can be determined using physical and psychological tests. Testing is important at this age if a child shows signs of possible retardation. In this present study it has been found that All Down children had high arsenic content may be due to high arsenic level of their parents.

Objective:
1. To identify trisomic Down syndromes and their families from our hospital.
2. To study the effect of environmental pollutions like arsenic in the etiology of the genetic disease especially Down syndrome.

Key Words:
Genetic counselling, Cytogenetics, Chromosomal abnormality, Arsenic.

Introduction:
Down syndrome (DS) is the most common and readily identifiable chromosomal condition associated with mental retardation. It is caused by a chromosomal abnormality: for some unexplained reason, an accident in cell development results in 47 instead of the usual 46 chromosomes. This extra chromosome changes the orderly development of the body and brain. In most cases, the diagnosis of Down syndrome is made according to results from a chromosome test administered shortly after birth. It is named after John Langdon Down, an English physician who published an accurate description of a person with Down syndrome. Therefore as a first step the genetic screening and diagnosis of Down syndrome in families of Index patients is being studied followed by genetic counseling.

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of a entire family to prevent the birth of a child with Down Syndrome.

Till now, 3000 inherited genetic diseases in humans have been reported. In addition to the clinical, biochemical and cytogenic detections that are available for some diseases, measurement of environmental toxicant like arsenic, lead of genetic disorder patient are necessary in the present day medical research.

Recent research into the toxic effects of arsenic have revealed that exposure to this environmental toxin has a pro-apoptotic effect on lymphoid cells. The mononuclear cells from children who have been chronically exposed to arsenic have a high basal rate of apoptosis.

Radiation, chemicals and other hazards in the environment can endanger the fetus. Chromosomal abnormalities are higher among the offspring of fathers exposed to high levels of radiation in their occupations. Environmental pollutants and toxic wastes are also sources of danger to unborn children. Among the dangerous pollutants and wastes are carbon monoxide, mercury and lead.

Arsenic has long been known to cause chromosomal damage, but most investigators have been unable to induce direct gene mutation. This apparent pardon, plus occasional poor convrelation between arsenic exposure dose and resultant frequency of chromosomal aberrations, has been explained by the concept that arsenic promotes genetic damage in large part by inhibiting DNA repair. The repair inhibition may be a basic mechanism for the comutagenicity and presumably the cocarcinogenicity of arsenic. Comparisons of chromosome aberration frequencies induced by trivalent and pentavalent arsenic have indicated that the trivalent forms are far more potent and genotoxic than the pentavalent forms.

Down syndrome disease condition has been reported with a high frequency and no therapy is available so it is essential to undertake genetic screening, molecular diagnosis and counseling in our country. The main aim of the study is to create awareness in the population about this disease and thus elimination of Down’s patients from the population. As different environmental pollution play a major role in the etiology of different genetic diseases. We would like to study whether there is any relationship with increased arsenic content and Down syndrome.

Materials and Method:

Identification of Down Patients and Their Families

The total number of cases (for last six months) of Karyotyping done in the cytogenetics unit of the Genetics Department of Ramakrishna Mission Seva Pratishthan is 78. Out of 78 cases 15 cases (19.23 %) were diagnosed as Down syndrome. The cases were referred from different Dist., Hospitals, Health Centers, Clinics of West Bengal and also Outdoor and Indoor Deptt. of Ramakrishna Mission Seva Pratishthan.

Cytogenetic analysis of the index patients:

Blood cultures were made for chromosome preparations as per routine procedures (Moorhead et al 1960, Sharma and Talukder 1974). Karyotyping was done on index patients. The banding technique was applied whenever necessary.

Measurement of arsenic level:

Arsenic level was measured from biological sample like hair.

Genetic Counseling:

Genetic Counseling was done with the help of counselors of Ramakrishna Mission Seva Pratishthan Hospital.
Results:

Table 1. Age of Mothers and Fathers and Distribution of Mothers Having Birth Wastage Before the Birth of the Down Syndrome Child

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>No. of mother</th>
<th>% present</th>
<th>Birth wastage</th>
<th>No. of father</th>
<th>% present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Abortion</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Spontaneous</td>
<td>Induced</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>one</td>
<td>two</td>
<td></td>
</tr>
<tr>
<td>15-20</td>
<td>1</td>
<td>6.67</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>21-25</td>
<td>6</td>
<td>40</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>26-30</td>
<td>4</td>
<td>26.67</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>31-35</td>
<td>2</td>
<td>13.33</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>36-40</td>
<td>2</td>
<td>13.33</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Inference:

Maximum number of Down syndrome cases was born to mother of age group 21-25 years and previous spontaneous abortion is a risk factor for giving birth to Down syndrome baby.

Table 2. Chromosomal Analyses of the Down Syndrome Cases

1000 blast cells were analyzed for each individual to study the aberration of chromosomes

<table>
<thead>
<tr>
<th>Age group</th>
<th>Trisomy 21(Pure)</th>
<th>Mosaicism</th>
<th>Translocation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>5</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>1 yr- 4 yr 11 months</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>5 yr- 9yr 11 months</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>10 yr- 14 yr 11 months</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15 yr- 19yr 11 months</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;20 years</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Inference:

Cytogenetic testing revealed that all the Down syndrome patients had pure trisomy 21. No mosaicism or translocation had been seen among 15 DS child.
Table 3. Down Syndrome Cases and Their Families From Different Areas and Their Level of Arsenic

<table>
<thead>
<tr>
<th>Different District of West Bengal</th>
<th>Kolkata</th>
<th>Howrah</th>
<th>24Pargana (S)</th>
<th>24Pargana (N)</th>
<th>Hooghly</th>
<th>Burdwan</th>
<th>Birbhum</th>
<th>Nadia</th>
<th>East Midnapur</th>
<th>Malda</th>
<th>Murshidabad</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Patients</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Arsenic (µg/kg) In Down syndrome patient</td>
<td>901.95</td>
<td>635.1</td>
<td>572.48</td>
<td>481.86</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1697.16</td>
<td>256.04</td>
<td>-</td>
<td>128.66</td>
</tr>
<tr>
<td>Arsenic (µg/kg) In Mothers</td>
<td>144.2</td>
<td>200.1</td>
<td>524.29</td>
<td>240.09</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1001.98</td>
<td>207.63</td>
<td>-</td>
<td>351.5</td>
</tr>
<tr>
<td>Arsenic (µg/kg) In Fathers</td>
<td>116.85</td>
<td>123.07</td>
<td>338.17</td>
<td>326.32</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>793.52</td>
<td>254.12</td>
<td>-</td>
<td>268.63</td>
</tr>
</tbody>
</table>

N.B- Normal level of Arsenic is 80-250 µg/Kg.
Toxic level of Arsenic is above 1000 µg/Kg.
Body burden level of Arsenic is 250-1000 µg/Kg.

**Inference:**
In case of Down syndrome patients and their parents arsenic content is not in toxic level but it is in alarming situation that is well above the normal range. Thus it can be said that maximum cases are having arsenic body burden.

**Discussion:**
Registries of congenital anomaly report 2-4% of births with congenital anomaly, depending on inclusion criteria and ascertainment methods. Cardiac defects account for over one-quarter of all cases, limb anomalies one-fifth, chromosomal anomalies and urinary system anomalies each around 15%, central nervous system anomalies including neural tube defects 10% and oral clefts 7%. The subgroups that have been most commonly singled out for specific study are neural tube defects, oral clefts and more recently cardiac defects and it is therefore unsurprising that these subgroups arise most commonly in reports of pollution-related effects. (Dolk and Vrijheid, 2003)

During the period 1995–99 for example, EUROCAT data from 32 European regions showed that 53% of spina bifida cases and 33% of Down syndrome cases were prenatally diagnosed leading to termination of pregnancy, averages which range from 0% in some regions to over 75% in other regions. The practice of
Prenatal screening has also brought forward the time of diagnosis of a range of internal congenital anomalies (cardiac and urinary system particularly) leading to increases in reported prevalence of these anomalies in recent decades.特别在有更多密集的筛查的地区 (EUROCAT Working Group. EUROCAT Report 8: Surveillance of Congenital Anomalies in Europe 1980–1999. www.eurocat.ulster.ac.uk; University of Ulster, 2002).

In a Hungarian village, 11 out of 15 live births in a 2-year period were affected by congenital abnormalities and six were twins. Four out of the 11 affected children had Down syndrome. Trichlorofon (an organophosphate pesticide) was used in excess at local fish farms, and local people were known to have eaten the local fish. No congenital abnormalities occurred in the 2 years after the chemical treatment of fish was banned. The study did not manage to establish a full explanation for the cluster of congenital anomalies in terms of fish consumption, but the evidence was suggestive that Trichlorofon was at least a partial explanation. (Dolkand Vrijheid, 2003).

The incidence of common congenital malformation at birth is considered to be a suitable method for ascertaining the effect of environmental agents on the population. Some may be due to teratogenic effects and others due to concurrent polygenic predisposing factors, but the majority of cases a cause and effect relationship is rarely detected. In the causation of neural tube defect for example, a definite genetic predisposition exist and certain populations are more susceptible than others. The finding that vitamin supplements in early pregnancy can prevent recurrence is also suggestive of environmental factors. In ICMR 1976 survey, a large number of foetal and neonatal deaths were screened and death rates were found to be due to malformations in 14.8 % and a further 24.6% due to unknown causes. Malformations have also found to be lower in patients having satisfactory antenatal supervision. One of the most significant finding has been the difference in occurrence of congenital defects in babies born to mothers with or without proper antenatal supervision (Master – Notani et. al. 1968). It appears from various surveys that cleft lip and palate, spinal defects, digital defects and gastrointestinal tracts defects are the commonest abnormalities found in newborns (Talukder and Sharma 1979, Verma 1997). The incidence of Down syndrome amongst autosomal defects appears to be around 1.5-2 per 1000 live-births Kochupillai et al. (1974) have shown that a possible cause of increased incidence in Kerala can be the high background irradiation.

For the last 15 years it has been shown that trisomy 21 is the commonest defect observed in Down syndrome and it occurs 1-2 per 1000 live-birth. The incidences of sex chromosomal anomalies account for a percentage of physical and mental handicaps are observed. Thus, it is apparent that human chromosome anomalies exit in India in number comparable to other countries (Talukder and Sharma 1979). The relationship to maternal age is not too clear in India where the majority of Down’s cases are born to the age group 20-29 years. A relationship to the time of birth has been suggested that the maximum affected children are born between January and March (Talukder 1979). Despite the the large number of potential mutagens like bacteria, virus, mycoplasma and others commonly found in India, none has so far been
correlated to congenital defects or chromosomal aberrations (Talukder 1979).

Chronic exposure of humans to high concentration of arsenic in drinking water is associated with skin lesion, peripheral vascular disease, hypertension, black foot disease and a high risk of cancer. Studies have shown that arsenic toxicity is the major problem of the south western district of West Bengal, India and Bangladesh where as many as 45 million people may be exposed to arsenic in drinking water, with 2.9% of the studied population already demonstrating a clinical manifestation of arsenic poisoning (Hadi and Parveen, 2004).

Epidemiological study in West Bengal, India has shown that there are 2,600 villagers covering 74 blocks where the ground water contains 50 µg/L arsenic and about 42.7 million in these 9 arsenic effected district are at risk (Rahman et al.; 2007). The persons identified recently in the previously cited areas with skin lesion have 467.8 ± 325.4 µg/L of arsenic in their urine with a background exposure of 342.7± 258.1 µg/L of arsenic in well water (Basu et al.2004). It is clear from the supported data given above that people of the selected areas of West Bengal, India have been exposed to increased Arsenic contaminated drinking water, and many of them shown chronic arsenicosis and different genetic disorder. In this present study it has been found that toxic level of arsenic of mother and arsenic level with body burden level of father had a DS child (age 10 months) with toxic level arsenic content. This high arsenic level is due to passage of arsenic from parents. All Down children had high arsenic content may be due to high arsenic level of their parents. The sample size is not enough to draw any conclusion but arsenic may have role of giving birth of Down syndrome baby.

Acknowledgements:
This study was financially supported by the grants from Department of Science & Technology (DST), West Bengal. We are grateful to the Secretary, Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences, Kolkata for the necessary permission to carry out this study.

Reference:


Introduction:

Respiratory distress syndrome (RDS), or hyaline membrane disease, remains a significant cause of neonatal morbidity and mortality, despite greater understanding of its pathophysiology and advances in perinatal care. It occurs almost exclusively in premature infants, with an incidence and severity inversely related to gestational age and birth weight. RDS complicates 1% of all births, but incidence rises to 50% at 30 weeks gestation, 75% at 28 weeks and 90% at 26 weeks. At gestations below this, RDS is almost universal.

The classic natural history of RDS sees development of respiratory distress either at birth or shortly afterwards with clinical deterioration over the first 48-72 hours of life. Provided that appropriate and timely medical support is initiated, subsequent improvement is then seen. Without intervention, and/or in the most severe cases, death can ensue as a result of progressive hypoxia and respiratory failure.

Pathophysiology:

Typical signs observed in an infant with RDS include grunting, cyanosis, tachypnoea and chest wall retraction. Plain chest radiograph images show a characteristic ground glass appearance, air bronchograms and diminished lung volume.

Fig 1: The left radiograph shows diffuse ground-glass appearance of lung fields. Blue arrows are indicative of air bronchograms. The right hand side image shows a normal neonatal chest X-ray.

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These observations are a result of complex pathological process beginning with inadequate (deficient and immature) surfactant production, leading to the formation of hyaline membranes within hours of birth. In more mature babies, and those with milder disease, endogenous surfactant production commence within a few days, leading to recovery.

For the remainder, recovery is slower and an inflammatory response ensues with subsequent risk of chronic lung disease (CLD). Extrapulmonary complications such as intra-ventricular haemorrhage (IVH), patent ductus arteriosus, sepsis, retinopathy of prematurity and neurological impairment are also observed.[2]

**Prevention Strategies:**
Several groups have an increased risk (male, multiple birth, infants of diabetic mothers,
caesarean section deliveries) but most infants developing RDS are born prematurely and there is often prior warning of impending delivery. The potential exists for obstetrics, midwifery and neonatal teams to adopt strategies to prevent RDS, or minimize its severity.[2]

**Antenatal Management:**
The great determinant of RDS incidence and severity is gestational age. Therefore the implementation of strategies to prevent premature delivery is of paramount importance. Provision of quality antenatal care and promotion of healthy maternal lifestyle can’t be overemphasized. Teenage pregnancy, social deprivation, poor nutrition and poor antenatal care and attendance are all associated with premature delivery and adverse neonatal outcome. Behavioural influences such as alcohol, smoking or recreational drugs are further risk factors.[2]

**Fig 3: Physiologic stress response in relation to preterm birth[3]**

**Timing of Planned Caesarian Section[4]:**
The risk of respiratory distress is increased following caesarean section deliveries and is multifactorial in origin.

Surfactant production and lung fluid clearance are enhanced by the onset of labour and triggered by β-adrenergic agents and prostaglandins. Advancing gestation increases the ratio of lecithin to sphingomyelin concentration in amniotic fluid, increases the concentration of surfactant protein and increases endogenous glucocorticoid production. These changes are delayed or diminished in infants who develop RDS. To a lesser degree, the physical process of labour also aids removal of lung fluid by compressing the chest. Consideration should therefore be given to the necessity and timing of planned caesarean section (CS) delivery.
Although the incidence of RDS in babies born after 36 weeks is low (2-3/1000), it mostly occurs in these infants when born by planned CS. A significant decrease in RDS and other respiratory morbidity is also seen with each completed gestational week until 39+6. The National Collaborating Centre for Women’s and Children’s Health and Royal College of Obstetrics and Gynaecology therefore recommend that planned CS should not be carried out before 39 weeks.\textsuperscript{[4]}

**Antibiotics:**

Antibiotics may delay delivery for women who enter labour prematurely. Activation of both innate and acquired immune systems, and increased pro-inflammatory cytokine levels are seen in labour, and can be prematurely triggered by infection. Infection may contribute to more than half of all cases of RDS in the most extremely premature infants.

The ORACLE trial of antibiotics for spontaneous preterm labour, and a Cochrane review assessing prophylactic antibiotics for inhibiting labour with intact membranes, found no evidence of reduced neonatal morbidity. There, the benefit of using antibiotics in asymptomatic women in preterm labour accompanied by rupture of membranes is less clear. Studies suggest that neonatal sepsis, intracerebral haemorrhage, and the need for oxygen and surfactant therapy are all reduced if peripartum antibiotics are used. However, mortality and longer term morbidity figures remain unchanged. The choice of antibiotic is controversial, but evidence of a correlation between the use of co-amoxiclav and necrotizing enterocolitis has led to recommendations for the use of erythromycin instead.\textsuperscript{[5]}

On the whole, there is no evidence that the use of antibiotics in preterm labour or preterm rupture of membranes reduces the risk of RDS.\textsuperscript{[5]}

**Tocolytics:**

Tocolytics can delay premature delivery, but there is no evidence that they can reduce perinatal or neonatal mortality, or neonatal morbidity including RDS. Advocates site a benefit of delaying delivery to allow the opportunity for women to be offered antenatal steroids and transferred to a unit with tertiary neonatal facilities. This greatly diminishes mortality and morbidity of extremely premature infants. In some instances such as cases of advanced labour or where there is evidence of intrauterine infection or placental abruption, tocolysis may be inappropriate. The Royal College Obstetrics and Gynaecologists (RCOG) currently recommend case-by-case decisions, following a discussion of the available evidence with the mother.\textsuperscript{[5]}

**Antenatal Corticosteroids:**

The development and widespread use of antenatal corticosteroids prior to premature delivery have had a substantial impact upon neonatal morbidity and mortality. The most recent Cochrane review showed an overall reduction in RDS and neonatal death, with the greatest benefit observed in infants born between 1 and 7 days after receiving corticosteroids. Infants born outside of this window had only a non-significant trend towards risk reduction. Additionally there appear to be added benefits of reductions in cases of IVH, necrotizing enterocolitis and early onset sepsis. Whilst antenatal corticosteroids do not confer any direct benefit to the mother, there are no apparent significant adverse effects either. Caution should be exercised with maternal systemic infection or overt chorio-amnionitis. However, the use of antenatal steroids in women at risk of preterm delivery is advocated as routine practise.
Whilst the advantages of corticosteroids are clear, several controversies remain, including the choice of drug, optimal dose, treatment window and the value of repeat dosing.

**Preparation and Dose:**

A 2006 Cochrane review of betamethasone versus dexamethasone, suggested that whilst both drugs significantly reduced RDS, a greater reduction was observed with betamethasone. A more recent review in 2008 found no differences in neonatal outcome, apart from a lower incidence of IVH with dexamethasone. No firm conclusions have been drawn regarding optimal route or precise regimes for administration, but the latest RCOG guidelines suggest betamethasone 12mg given intramuscularly in two doses, or dexamethasone 6 mg given intramuscularly in 4 doses should be the standard practise.

**Fig 4:** Maximum risk reduction for RDS is seen if ANS is given between 1 & 7 days before delivery. Likewise it is the risk of neonatal death that is most reduced in the event of administration of antenatal steroids[6]

<table>
<thead>
<tr>
<th>Overall</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;34 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;31 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 &amp; &gt;7 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 - 168h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>0.1</th>
<th>1</th>
</tr>
</thead>
</table>

**Which Gestations:**

In maternally corticosteroid treated infants, combined foetal and neonatal death is significantly reduced in those born between 28 and 36 weeks, and RDS is significantly reduced in those born between 28 and 34 weeks gestation. There is paucity of data for the use of steroids in pregnancies below 26 weeks, with no clear evidence of a reduction in RDS. However, there is evidence to suggest a reduction in other neonatal outcomes and longer term neurodevelopment, and so the use of steroids from 24 weeks is generally supported.

Below 24 weeks, less agreement exists. A 2008 study of infants born at 23 weeks, showed a reduced risk of death in infants receiving full course of antenatal steroids compared to those receiving none. The decision to offer steroids
The ASTECS research team looking at the effects of antenatal steroids for elective CS at term, found a decrease in NICU admission, overall respiratory morbidity, and RDS in the group randomized to antenatal steroids. Whilst elective CS below 39+0 weeks gestation should not be routine practise, the RCOG recommend the use of antenatal steroids until 38+6 weeks where a CS is planned. For all other modes of delivery, the administration of antenatal steroids for pregnancies over 34+6 weeks is not supported.

**Repeat Dosing:**
As the efficacy of antenatal corticosteroids is reduced if birth has not occurred within 7 days of administration, there has been much debate over the issue of repeat dosing.

Observational studies offer conflicting results, with some suggesting adverse effects on foetal and early childhood development in those receiving multiple steroid courses. At the same time, there have been suggestions of reduced rate of cerebral palsy. More recent randomized controlled trials also offer conflicting results with regard to RDS incidence and other neonatal morbidity.

A 2011 Cochrane review of mothers who received repeated courses of betamethasone, found a risk of reduced risk of RDS and reduced mechanical ventilation, oxygen and surfactant use, despite a mean reduction in birth weight of 76g. No longer term outcome differences were observed.

The authors therefore concluded that the use of repeat doses of steroids for women still at risk of preterm delivery 7 days after the initial course could be supported. There is not however, an agreement on the frequency of repeat dosing, with regimes differing between every 7-14 days or rescue therapy whereby repeat courses are only given if delivery is deemed imminent.

There are no thorough reviews of multiple dexamethasone courses, or studies looking at repeat dosing specifically in multiple pregnancies, although one randomized controlled trial in twin pregnancies, did find a significantly reduced risk of RDS in those receiving rescue doses.

The most recent RCOG guidance (prior to Cochrane review) does not recommend weekly repeat courses, but does advocate consideration of a single course in pregnancies where the initial course was given before 26 weeks.[5]

**Perinatal Management:**
Avoidance of planned pre-labour CS below 39 weeks will reduce RDS incidence in late preterm and early term infants.[4] Incidence of RDS is not uncommon in late preterm babies. Where premature labour does occur, labour ward conditions should be optimized to curtail the occurrence and severity of RDS. There is some limited evidence to suggest that delivery in a unit with on-site tertiary neonatal facilities can improve outcome in the most premature infants. As in utero transfer will not always be possible, each maternity unit should have a policy in place to allow provision of effective neonatal resuscitation, and coordination of early neonatal transfer where appropriate.

**Facilities - Warmth:**
The viability of the newborn to achieve thermoregulation is restricted in the first few hours of life, becoming more difficult with reducing gestational age and weight. Preventing heat loss in preterm infants improves survival, and strategies should be implemented from the outset.
Hypothermia produces a specific risk for worsening RDS by reducing production, secretion and function of surfactant, thus increasing the risk of both primary and secondary surfactant deficiency. Cold stress is also associated with acidosis and hypoxia.

Heat loss occurs via all modes of heat exchange (conduction, convection, radiation and evaporation) and is heavily influenced by the surrounding environment. The most important element in preterm infants is evaporative loss of amniotic fluid from the skin. This can be reduced by the use of plastic bags in babies less than 28 weeks gestation. Furthermore, simple approaches such as maintaining delivery room temperature at a minimum of 26°C, the provision of warm blankets (and replacing wet blankets with dry ones), minimizing draft sources, and pre-warming resuscitation equipment and surfaces should be undertaken as routine. At delivery, infants should be dried (unless using plastic bags), wrapped and placed either under a radiant warmer or in skin to skin contact with the mother immediately.

**Resuscitation:**

Optimal management at delivery improves neonatal outcome and reduces respiratory morbidity. Newborn life support guidelines published by the resuscitation Council UK detail equipment that should be present at delivery and advice on management of babies requiring resuscitation/assisted transition from foetal life. Surfactant deficient lungs may require greater inflation pressures and times to achieve adequate tidal volumes and alveolar aeration. It is important to ensure that tidal volumes are regulated to avoid atelectasis or volutrauma if they are too low or high respectively. Bag and mask ventilation has largely been replaced by the use of T-piece devices which enable a stable and adjustable positive end expiratory pressure and peak inspiratory pressure.\[7\]

Blended air and oxygen circuits should be used with caution and in conjunction with pulse oximetry readings taken from the right hand (preductal). Acceptance of oxygen saturation levels of 60% at 2 minutes of life, 85% at 5 minutes, and 90% at 10 minutes should prevent inappropriately aggressive oxygen therapy and its associated toxicity.\[7, 8\]

Growing evidence exists that the administration of early delivery room CPAP for infants at risk of RDS leads to reduced respiratory morbidity and pneumothorax, and reduced neonatal morbidity. Where babies do not respond to CPAP, intubation and positive pressure ventilation are required.\[5\]

**Surfactant:**

Like antenatal steroids the use of surfactant has been pivotal in advancing perinatal medicine over the last few decades. Surfactant reduces respiratory morbidity, pulmonary air leaks, and death but uncertainty exists over the optimal dosing and timing of administration and which preparations and modes of administration are most suitable.
Without Surfactant small alveoli are not stable and copapase into larger ones because $P_1 >> P_2$.

Without Surfactant alveoli are stable regardless of their size.

**Fig. 5: Alveoli with and without surfactant**

**Who For:**

Improvements in neonatal outcome have been constantly shown for infants receiving surfactants from around 25-32 weeks. Reliable evidence outside this window is lacking, and it would be difficult to justify randomized controlled trials of surfactant in the most extremely premature infants. However, whilst the impact on mortality rates for more immature infants is uncertain, there do appear to be short term advantages in the level of respiratory support required, making the use of surfactant for such infants routine.

For the infants of more advanced gestation, a paucity of quality evidence makes recommendations more difficult but most agree that infants with clinical and radiographic evidence of RDS with significant respiratory support requirements should be treated with surfactant.

**Type** – Both natural and synthetic surfactant preparations have been used in the treatment of RDS although at present only natural forms are used across Europe. While both are effective in treating RDS, the use of natural products result in fewer pulmonary leaks, deaths and number of days of ventilator support. Although there is a slight increase in milder forms of IVH with natural forms, there are no other apparent drawbacks when compared to synthetic products and as such natural products are the current products of choice for RDS management.[9]

Porcine preparations appear to confer some...
advantages over bovine preparations in terms of need for repeat dosing, volume required and effects on mortality but make no significant difference on the impact of BPD. The current level of evidence is insufficient to draw firm conclusions.\textsuperscript{[9]}

Table 1: Trials comparing different Natural Surfactants: \textsuperscript{[10]}

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Surfactants Used</th>
<th>Participants</th>
<th>Endpoints of Trial</th>
<th>Results of Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Ramanathan \textit{et al.}</td>
<td>1. Beractant 2. Poractant Low dose 100mg/kg High dose 200mg/kg</td>
<td>293 &lt;35 weeks GA BW750-1750g</td>
<td>1. $O_2$ requirement at 36 first 6 hours after dosing 2. Pneumothorax 3. $O_2$ requirement at 36 weeks 4. Mortality rate</td>
<td>High-dose poractant lower mortality rate Other endpoints same</td>
</tr>
<tr>
<td>2005</td>
<td>Malloy \textit{et al.}</td>
<td>1. Beractant 2. Poractant High dose 200mg/kg</td>
<td>60 &lt;37 weeks GA with RDS</td>
<td>1. Pneumothorax 2. BPD at 36 weeks 3. Mortality rate</td>
<td>No difference in endpoints</td>
</tr>
<tr>
<td>2011</td>
<td>Singh \textit{et al.}</td>
<td>1. Beractant 2. Poractant Low dose 100mg/kg High dose 200mg/kg</td>
<td>529 &lt;37 weeks GA with RDS</td>
<td>1. $O_2$ requirement at 36 weeks 2. Need fir re-dosing 3. Short-term outcome 4. Mortality rate</td>
<td>Poractant reduced need of re-dosing, improved short-term outcome, and decreased mortality $O_2$ requirement at 36 weeks same for both groups</td>
</tr>
<tr>
<td>2011</td>
<td>Ramanathan \textit{et al.} \textit{(Retrospective study)}</td>
<td>1. Beractant 2. Poractant 3. Calfactant</td>
<td>14,173 &lt;37 weeks GA with RDS</td>
<td>Mortality rate</td>
<td>Poractant significantly reduced mortality as compared to calfactant Poractant insignificantly reduced mortality as compared to beractant.</td>
</tr>
</tbody>
</table>
Dosing and Repeat Courses:
Each manufacturer recommends slightly different dosing regimens, and there are limited studies assessing the optimum choice. In preterm babies, a dose of 200mg/kg of porcine surfactant appears beneficial over 100mg/kg for moderate/severe RDS, with fewer re-treatments and better oxygenation.

With regard to repeat doses of surfactant, few randomized controlled trials exist. These demonstrate reduced mortality and need for ventilator support as well as improvements in oxygenation, and reduction in incidence of pulmonary air leak and necrotizing enterocolitis. Though there is no apparent benefit in prophylactic multiple dosing, targeted repeat treatments for deteriorating infants who had previously shown a good response to surfactant makes sense.

Timing: Prophylaxis, Early or Delayed:
Prophylactic administration generally refers to surfactant use immediately after delivery-either before or just after the first breath. Treatment or ‘rescue’ surfactant describes administration at an undefined period of time after birth, once clinical evidence of RDS is observed.

Both strategies improve neonatal outcome. Theoretically prophylactic treatment replaces surfactant before the onset of respiratory difficulty, allowing the duration and level of ventilation support to be reduced along with the degree of barotraumas that results. Animal models have also demonstrated a more uniform distribution and reduced pulmonary inflammation with this approach. However, this involves the risk of intubating and treating babies who would not otherwise have developed RDS or needed mechanical ventilation and necessarily has cost implications.

Early studies suggested a reduction in BPD death and pulmonary air leak in those receiving prophylactic treatment. However these studies were from an era before the widespread use of antenatal steroids, a more gentle approach to resuscitation and the routine initiation of early nasal CPAP. More recent meta-analysis include trials where such practises are employed. On evaluating this evidence, we see that whilst prophylactic treatment is still favourable without the routine application of CPAP, the same benefit is not seen when CPAP is employed.[5]

With modern perinatal practices, selective early surfactant treatment of babies who developed respiratory distress requiring intubation, irrespective of gestation, seems a more balanced approach than routine prophylaxis. It is reasonable to assess the baby at delivery and perform initial resuscitation before deciding to administer surfactant. This will avoid unnecessary intervention in those who would not otherwise develop significant RDS, without prejudicing neonatal outcome in those who would.

Early CPAP Versus Surfactant:
Recent studies have focussed on whether the routine use of early CPAP could avoid a need for surfactant therapy. Some centres and authors have indeed demonstrated that expert use of CPAP can reduce the need for surfactant entirely in some groups of infants. The SUPPORT trial looked at infants from 24 weeks gestation and randomly assigned to either treatment with nasal CPAP or combined intubation and surfactant within an hour of birth. A higher rate of subsequent intubation and surfactant treatment was observed in the former group, but no difference in death or BPD was shown. However,
there was a reduction in the need for postnatal corticosteroids and duration of mechanical ventilation in the CPAP group, without adversely affecting neonatal outcome.

Otherwise studies have shown that the early use of CPAP (i.e. immediately from birth) in babies at risk of RDS can reduce its severity by decreasing the need for surfactant and mechanical ventilation. The use of CPAP post extubation also reduces the need for re-intubation and improves clinical outcome for babies treated for RDS.[9]

**Neonatal Management:**

For infants with established RDS, a number of clinical considerations are needed to optimize care and reduce the impact of RDS, as well as prevent the development of BPD. A thorough overview of practices is beyond the scope of this article but there is existing guidance from the British Association of Perinatal Medicine as well as European consensus guidelines on the management of neonatal RDS.

Strict maintenance of body temperature, ensuring adequate nutrition and close monitoring and early intervention with sepsis are important aspects of general neonatal care. Whilst lung oedema is a common finding in RDS, there is no evidence that fixed fluid restriction has any impact on outcome. However as the normal pattern of diuresis may be delayed in RDS, attention to oedema, fluid and sodium balance should be practised to avoid fluid overload as this will negatively impact upon the development of BPD, and can worsen a PDA.

In terms of drug treatment, there is no evidence to support the routine use of diuretics and there is insufficient evidence that treating PDAs reduce the severity of RDS. Following data from CAP Study, early caffeine treatment is felt to be beneficial in reducing BPD.[11]

Regarding ventilator strategies, the development of BPD is multi-factorial, but the need for invasive ventilation in itself is a risk factor. The aim should be to avoid mechanical ventilation if possible, with an aggressive approach to weaning where appropriate. Whilst volume targeted ventilation appears to confer benefits over pressure-based approaches, there is no evidence that any specific mode of ventilation is superior in reducing medium to long term respiratory morbidity in patients with RDS.[12]

**Conclusion:**

The development and progression of RDS can be minimized by a structured, evidence based approach. As majority of severe cases occur in premature infants, combined obstetrics and neonatal strategies aimed at preventing premature delivery, together with optimization of maternal condition (including the use of antenatal steroids) offer the best chance of avoiding neonatal respiratory morbidity. Where premature delivery occurs, it should take place with expert personnel present and with appropriate delivery room facilities and equipment in place. A targeted approach to surfactant therapy, including repeat doses where necessary should be employed together with a systematic approach to early newborn care. Use of rescue surfactant and labour room CPAP improves the outcome.
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A Comparative Study on The Use of Intranasal Steroid Spray in Allergic Rhinitis & Allergic Fungal Rhinosinusitis

Dr. Soumitra Ghosh¹, Dr. A. Roychowdhury², Dr. B. K. Roychaudhuri³

Introduction:
Allergic rhinitis (AR) is a chronic respiratory disease that is frequently associated with bronchial asthma. AR is one of the top-10 reasons for patients to visit their primary care physicians¹,² in the western world. The first-line therapy for AR according to ARIA guidelines is intranasal corticosteroids (INS) along with oral antihistaminics³.

Allergic Fungal Sinusitis (AFS) is a clinical condition believed to manifest due to an allergic reaction to aerosolized environmental fungi, usually of the dematiaceous species, and that too in an immune-competent host. Approximately 5-10% of patients of chronic rhinosinusitis actually suffer from AFS. Atopy is characteristic of AFS; approximately two thirds of patients report a history of AR, and 90% demonstrate elevated specific IgE levels to one or more fungal antigens. Surgical clearance of the disease along with prolonged therapy with anti-inflammatory agents in the form of oral corticosteroids and INS help prevent recurrence. Immunomodulators have also being tried to prevent recurrence in AFS patients.

This review article provides comparative information on INS medications for the effective management of AR & AFS, and to identify the factors that may affect the initial selection of an INS by the treating physician.

Pathophysiology:
The different phases of AR include sensitization, early-phase reaction, and late-phase reaction. Sensitization occurs due to the initial exposure of the respiratory mucosa to an allergen which is (IgE) immunoglobulin mediated.⁴ On re-exposure mast cells and basophils release chemical mediators such as histamine, tryptase, heparin, leukotrienes, and cytokines. This results into mucus secretion and other manifestations of allergic rhinitis.⁴ Over the next few hours inflammatory cells such as eosinophils and TH2 lymphocytes release additional mediators that cause tissue damage and promote the amplification of the allergic response (late-phase response).⁴

The pathophysiology of AFS is thought to be similar to that of allergic bronchopulmonary fungal disease (a term replacing bronchopulmonary aspergillosis). An atopic host, when exposed to fungi through normal nasal respiration, triggers the initial antigenic stimulus. The initial inflammatory response occurs as a result of IgE-mediated and type III (immune complex–mediated) reaction resulting in tissue edema. This leads to subsequent obstruction of sinus ostia, which may be aggravated by anatomic factors such as septal deviation or turbinate hypertrophy, thereby resulting in stasis within the sinuses. Thus an ideal environment is created for further proliferation of the fungus and increased antigenic exposure to the patient. Eventually allergic mucin, the material that fills the involved sinuses, is produced in abundance and accumulation of the debris obstructs the involved sinuses and propagates the process.

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Clinical response:
The common symptoms of AR include sneezing, rhinorrhea, nasal itching and nasal congestion. They may be associated with itching, redness and watering of the eyes also. These clinical features may lead to fatigue, irritability, and mood fluctuations resulting in poor quality of life.[5] Previously AR was classified as seasonal (SAR: caused by seasonal allergens) or perennial (PAR: caused by environmental allergens throughout the year) based on the frequency and timing of symptoms.[6] The Allergic Rhinitis and its Impact on Asthma (ARIA) working group, together with the World Health Organization (WHO), has implemented a classification system for AR based on persistence (intermittent or persistent) and severity (mild, moderate to severe) of symptoms.[3] They have also recommended guidelines for proper management of these severity based classifications of AR.[3] Therapies for the treatment of AR include H₁-antihistamines, decongestants (systemic and intranasal), mast cell stabilizers (cromones), anticholinergics, antileukotrienes, and INS.[7] Though each of the above modalities of treatment has demonstrated some effectiveness for treating various symptoms of AR, INS is the most effective treatment option for alleviating the greatest number of AR symptoms.[7, 8] INS control both early-phase allergic reaction and the late-phase inflammatory reaction caused by infiltration of the nasal mucosa with activated eosinophils and lymphocytes.[9] The ARIA guidelines recommend INS as the first-line therapy for persistent AR that is more than mild intermittent in severity.[3]

Patients with AFS usually present with features of nasal airway obstruction, allergic rhinitis or chronic sinusitis that include nasal congestion, purulent rhinorrhea, postnasal drainage, or headaches. They may typically complain of gradual nasal airway obstruction and production of semi-solid nasal crusts also known as allergic fungal mucin. Management of AFS depends on complete removal of all fungal mucin (usually requiring surgical clearance) and long-term prevention of recurrence through either immunomodulation (immunotherapy and/or corticosteroids) or fungistatic antimicrobials. Long term oral corticosteroids play the key role in controlling the inflammatory response and thereby preventing further recurrence. INS also plays an important role in controlling the disease, mainly in the postoperative period, as it can reach the nasal mucosa uniformly after surgical clearance of the pathology.

Intra Nasal Steroids:
Mechanism of action: It is not well established whether INS penetrate the nasal mucosa or act on target cells. The mediators which are affected include prostaglandins, leukotrienes, TH₂ cells and mast cells.[10] The rationale for topical corticosteroids in the treatment of AR & AFS lies in achieving adequate drug concentrations at receptor sites locally in the nasal mucosa which leads to symptom control and reduces the risk of systemic side effects.[10-12]

Potency: Six INS molecules are available for the treatment of AR in the United States: beclomethasone dipropionate, flunisolide, budesonide, fluticasone propionate, mometasone furoate, and triamcinolone acetonide. The topical potency of corticosteroids is usually determined by the degree of cutaneous vasoconstrictive activity and glucocorticoid receptor-binding affinity. One study determined a rank order of receptor-binding affinity (lowest to highest) to be dexamethasone, triamcinolone
Acetonide, budesonide, fluticasone propionate, and mometasone furoate.\[13\] In a similar study, fluticasone had higher affinity than the active metabolite of beclomethasone, dexamethasone and budesonide.\[14\]

Highly lipophilic agents have a higher and faster rate of absorption into the nasal mucosa and therefore increased ability to reach the glucocorticoid receptor due to longer retention time in nasal tissue.\[15, 16\] In one study the order of lipid solubility of INS from lowest to highest was found to be flunisolide, triamcinolone acetonide, budesonide, beclomethasone dipropionate, fluticasone propionate, and mometasone furoate.\[17\] Performance of the inhaler devices also can influence lipophilicity characteristics and systemic bioavailability.

All INS, with the exception of beclomethasone dipropionate, are rapidly metabolized into inert compounds and, therefore, do not induce significant systemic effects.\[24\] Budesonide aqueous nasal spray, fluticasone propionate nasal spray, mometasone furoate nasal spray, and triamcinolone acetonide aqueous nasal spray are available in a once-daily dosing schedule which improves patient compliance. Several double-blind, placebo-controlled studies have shown that these INS sprays are more effective than placebo for the treatment of AR.\[19\] Multiple studies have suggested that most of the INS comparisons are equivalent in respect to efficacy and tolerability.

**Side effects:** A major concern of INS is their ability to cause systemic adverse reactions. Systemic absorption can be either due to absorption through the nasal mucosa or swallowing a fraction of the dose and absorption through the gastrointestinal tract.\[15, 21, 22\] Mometasone furoate and fluticasone propionate have very low systemic bioavailability, 0.1% and less than 2%, respectively, and are believed to be poorly absorbed into systemic circulation due to high lipophilicity.\[22\]

The hypothalamic-pituitary-adrenal (HPA) axis function has been measured to determine the drugs' systemic activity. No significant HPA suppression was noted with beclomethasone dipropionate 200-800 µg/day, triamcinolone acetonide 220 µg/day, fluticasone propionate 200 µg/day and mometasone furoate 200 µg/day.\[23, 26\] The dynamic function of the INS (measured by evaluating adrenocorticotropic stimulation) also showed no significant effects with beclomethasone dipropionate 336 µg/day, fluticasone propionate 200 and 400 µg twice/day, or triamcinolone acetonide 220 and 400 µg/day.\[27, 29\] These studies suggest that the drugs have little or no effect on the HPA axis when administered at recommended dosages.

Therapy with INS may result in some form of local reactions like nasal irritation, dryness, burning and stinging, and sneezing, headache and epistaxis in 5-10% of patients irrespective of the molecule.\[15, 30, 31, 32, 35\] Septal perforations, though rare, can be avoided by counseling patients on proper methods of administration of tilting the spray away from the septum and avoiding trauma from the delivery tip.\[21\] There are occasional reports in the literature of contact dermatitis on the nose, cheeks, and upper lip from budesonide nasal spray.\[36\]

**Safety Profile:**

INS scores over oral corticosteroids in terms of relatively short half-lives, topical activity, and rapid first-pass hepatic metabolism.\[37\] These factors help decrease systemic side effects of
INS. Current doubleblind, placebo-controlled studies have demonstrated that all once-daily INS are well tolerated for the treatment of AR. Though there are no long-term comparative studies of the once-daily INS on growth velocity in children; placebo-controlled studies of Budesonide and Fluticasone Propionate have shown no significant effects on growth velocity in children even after 1 year of treatment.\textsuperscript{[38, 39]} Budesonide has been shown to be safe to use during pregnancy (US FDA approved Category B)\textsuperscript{[40, 41]} supporting that budesonide treatment doesn’t pose any harm to the fetus.\textsuperscript{[42]} All other once-daily INS has been classified as Pregnancy Category C by the US FDA due to lack of evidences and studies.\textsuperscript{[42]} The dosage schedule and bioavailability of different INS molecules have been depicted in Table 1.\textsuperscript{[43,49, 45-51, 52-55]}

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Administration</th>
<th>Dosage</th>
<th>Age Group</th>
<th>Bioavailability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beclomethasone</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 spray/nostril 2-4 times/day</td>
<td>168-336 μg/day</td>
<td>Adults and children ≥ 12 yrs</td>
<td>Unknown</td>
</tr>
<tr>
<td>42 μg/spray</td>
<td>1-2 sprays/nostril twice/day</td>
<td>168-336 μg/day</td>
<td>Adults and children ≥ 6 yrs</td>
<td></td>
</tr>
<tr>
<td><strong>Budesonide</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 sprays/nostril twice/day or 4 sprays/nostril/day</td>
<td>256 μg/day</td>
<td>Adults and children ≥ 6 yrs</td>
<td>20</td>
</tr>
<tr>
<td>32 μg/spray</td>
<td>1-2 sprays/nostril twice/day</td>
<td>256 μg/day</td>
<td>Adults and children ≥ 6 yrs</td>
<td></td>
</tr>
<tr>
<td><strong>Fluticasone</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2 sprays/nostril/day or 1-2 sprays/nostril/day</td>
<td>200 μg/day 100-200 μg/day</td>
<td>Adults and children ≥ 12 yrs Children 4-11 yrs</td>
<td>0.5-2</td>
</tr>
<tr>
<td>50 μg/spray</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mometasone</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2 sprays/nostril/day or 1 spray/nostril/day</td>
<td>200 μg/day 100 μg/day</td>
<td>Adults and children ≥ 12 yrs Children 3-11 yrs</td>
<td>0.1</td>
</tr>
<tr>
<td>50 μg/spray</td>
<td></td>
<td></td>
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</tbody>
</table>

Table 1: Intranasal Corticosteroid Dosing Guidelines and Bioavailability

**Conclusion:**

There is little difference in the efficacy between the different INS currently available in the market. All INS are more or less well tolerated with similar short-term safety profiles. The differences among them are usually limited to patient preference, dosing regimens, and the delivery device and vehicle. Mometasone furoate and fluticasone propionate are more topically potent than the other agents. They have higher
lipophilicity, resulting in faster rate of absorption, longer retention time in the nasal tissues, and minimal absorption in the gastrointestinal tract. The bioavailability of these two drugs is minimal, which reduces systemic side effects. The drugs are equal to each other in terms of potency and superior to placebo in reducing total nasal symptoms, therefore leading to greater numbers of symptom-free days. When considering patient preference mometasone and fluticasone are dosed once/day and can be used by adults and children above 3 and 4 years of age, respectively.

Reference:


Truncal Desquamation in a Case of Kawasaki Disease

Dr. S. Guha1, Dr. D. Mondal2, Dr. S. Basu3, Dr. N. Mukherjee4, Dr. D. Mukherjee5

Abstract:
Kawasaki Disease (KD) is one of the most common vasculitides of childhood. Diagnosis of KD is mostly based on clinical suspicion. However problem arises in those cases where all the typical clinical features are not present. Here we present a case of incomplete KD where skin desquamation occurred (on tenth day of illness) mainly over trunk and forehead in contrast to typical periungal and perianal peeling.

Introduction:
KD is a vasculitis affecting mainly the medium and small sized arteries. It is characterised by systemic inflammation that manifests as fever, mucositis (mainly oral), bilateral non-purulent conjunctivitis, changes in peripheral extremeties and cervical lymphadenopathy. The diagnosis is sometimes difficult because all the clinical features may not be present at the same time. The disease though self limiting can cause serious cardiac complications and therapy in the form of Intravenous Immunoglobulin (IVIG) and aspirin should be initiated as soon as possible.

Case Report:
A four year male child born out of non consanguinous marriage, with normal growth and development presented with history of high grade fever for five days. This was associated with several episodes of vomiting.

On examination the child was febrile, irritable and had a facial flush. There was a polymorphous erythematous rash over the trunk and extremeties. Examination of the other systems was essentially normal.

Initial blood examination showed haemoglobin (Hb) 11.4gm/dl, total leucocyte count (TLC) 10,100/cumm (P88, L6, M2, E4), platlets 2.2l/cumm. C –reactive protein (CRP)-12mg/dl, erythrocyte sedimentation rate (ESR)-30mm in 1st hour. Liver function tests, urea, creatinine and serum electrolytes were within normal limits. Dengue serology and malarial dual antigen were negative. Urine and blood cultures were sterile.

A provisional diagnosis of viral exanthematous fever was made and the child was given symptomatic treatment with antipyretics. But however fever continued and the child became very irritable. On 7th day of fever he developed left sided tender jugulodigastric lymphnode. There was redness of the oral mucosa with fissuring of lips. Examination of the neurological system did not reveal any abnormality.

A repeat blood examination showed Hb-8.8gm/dl, TLC-25,000/cumm (N75, L22, M1, E2), platlets-3.5l/cumm, CRP-24mg/dl, erythrocyte sedimentation rate (ESR)-60mm, serum albumin-2.5gm/dl and serum albumin-135mmol/l. Serum transaminases, blood urea and creatinine were normal. Urine routine examination showed 10-15 pus cells/high power field but culture was sterile. Infective serology (brucella, rickettesia) were negative.
In the background of continuing fever with rash, mucositis, tender cervical lymphadenopathy and raised inflammatory markers along with sterile pyuria a provisional diagnosis of incomplete KD was suggested. Electrocardiogram showed tachycardia with low voltage complexes and ST inversion suggestive of myocarditis. Echocardiography (echo) on 8th day of fever revealed perivascular cuffing with bright prominent coronary arteries. There was no dilatation or aneurysm of the coronaries IVIG-at a dose of 2gm/kg along with aspirin @ 100mg/kg were started. The child became afebrile after 48 hours. On 10th day of illness he developed peeling of skin over forehead and trunk. There was no evidence of periungal desquamation. The child was discharged with aspirin @5mg/kg/d and suggested follow up echo at 4 weeks.

![Figure 1- Desquamation in the Forehead](image1)

![Figure 2 - Desquamation in the Trunk](image2)

**Discussion:**
Pediatric vasculitides are a diagnostic and therapeutic challenge. KD, a medium vessel vasculitis is now considered to be one of the commonest vasculitis in children[1]. It is one of the leading cause of acquired heart disease in children[2]. Diagnosis of KD is based on a typical temporal sequence of clinical features, none of them individually having any diagnostic significance. These clinical features evolve over a period of days and the entire spectrum is not seen at any particular point of time.

Criteria for diagnosis of KD has not changed much in 36 years, since the disorder was initially discovered.

Criteria for diagnosis of KD are —
Fever for 5 days or more with atleast 4 of the following clinical features not explained by any other disease process.
1. Bilateral conjunctival injection (80-90%) cases.
2. Changes in oro pharyngeal mucous membrane including one or more of (injected fissured lips / strawberry tongue / injected pharynx.)
3. Changes in peripheral extremeties including erythema / edema of hands / feet in the acute phase which later on gives way to periungal desquamation in the convalescent phase.
4. Polymorphous rash, primarily truncal, non vesicular.
5. Tender cervical usually unilateral lymphadenopathy >1.5cm.

These clinical features if present in a febrile child should point towards the diagnosis of KD. However dilemma arises in incomplete cases of KD where along with fever only 2/3 of the 5 clinical features are present. One has to then take the help of laboratory criteria (raised inflammatory markers).[3]

As already mentioned all the typical clinical features may not be present at any particular time. Infact they evolve over a period of time, as had happened in our case.

Initially there was only fever with rash and normal inflammatory markers, which mislead us to a diagnosis of viral exanthematus fever. But the development of tender cervical lymphadenopathy with oral mucositis prompted us to think of an alternative diagnosis. Since only 3 out of 5 clinical features were present, incomplete KD was a possibility. This was further supported by raised inflammatory markers with sterile pyuria and negative infective serology. Finally echo on 8th day showing affection of coronary arteries supported our diagnosis.

Desquamation in KD typically occurs after 10 days of fever and usually begins at the tips of toes and fingers just below the distal edge of nails (periungal). Perianal peeling is characteristically seen in KD [4]. As skin peeling is a late manifestation, it is more useful for retrospective diagnosis than for making therapeutic decisions.

In our case surprisingly skin peeling occurred over forehead and trunk (fig 1 & 2), sparing the toes and fingers. Only one case of truncal desquamation in KD has been reported by Cox J et al [5] in an 11 year male child where delayed diagnosis of KD was made after multiple visits to the pediatric department.

Our main purpose of presentation of this case are —
1. Clinicians when treating a febrile child with rash should not always presume it to be viral exanthema. One should carefully observe the child over a period of time, for appearance of other clinical signs especially if fever persists in an irritable child.
2. Peeling of skin in KD though typically occurs in toes, fingers and perianal region one must also look for desquamation at other sites.
3. It is essential to make diagnosis of KD preferably in the acute phase phase as early initiation of treatment with IVIG and aspirin may reduce the risk of cardiac complications.[3]

References:
A Rare Association Between Adult Onset Still's Disease & Dermatomyositis

Dr. S. N. Burman¹, Dr. P. Chakraborty², Dr. S. Mazumdar³, Dr. R. Rajak⁴

Abstract:
Adult onset Still’s disease is a rare systemic inflammatory disease characterised by classical triad of persistent high spiking fever, joint pain and a distinctive salmon coloured rash. The disease is considered a diagnosis of exclusion[1]. Level of Iron binding protein ferritin may be elevated with this disorder. There is rare association between dermatomyositis and AOSD. The present case was previously diagnosed as dermatomyositis but now presented as AOSD. Prognosis is usually favourable but manifestation of disease affecting the lung, heart or kidney may occasionally cause severe life threatening complications[2].

Case Report:
A 48 years old male patient admitted in RKMSP in August 2014 with chief complaints of high grade intermittent fever. He was also complaining of arthralgia for last 14 days and sore throat for the same duration. He was previously diagnosed as a case of dermatomyositis (proved by muscle biopsy) in the year 2009. But he lost follow up. There was past history of diabetes. At the time of admission, patient also presented with dry cough and on examination he was tachypnaec, febrile. There was congestion over the posterior pharyngeal wall, but no lymphadenopathy was found and on examination of the respiratory system there were coarse crepitations in the left infrascapular region of chest and in abdomen, there was hepatosplenomagaly. Patient was initially treated with injection ceftriaxone and Tab Azithromycin. But fever was not subsided. After 4-5 days of initial treatment patient was subsequently switched over to piperacillin and tazobactum keeping in view of underlying ongoing sepsis due to presence of high fever and high leucocyte count (TLC-21600, N86%, L10%, M2%, E2%). Subsequently there was appearance of purple coloured patch at the time of high grade fever appeared all over the body specially trunk and proximal part of lower limbs on 6-7th day of admission which was pruritic and non tender in nature. Rash used to disappear when the fever subsided. Blood for culture and sensitivity test was already sent on 1st day of admission which showed no growth. In the mean time serum procalcitonin level was done but not raised significantly. Blood for malaria parasite dual antigen and Dengue IgM and IgG were subsequently sent, and found all negative. At the 8th day of admission Blood for ANA, RA and serum Ferritin were sent, keeping in mind of other causes of fever. Blood for ANA and RA factor were negative but Serum ferritin was markedly high around 10300. Serum CPK was about 80 And CRP was 24 (positive). Fever did not subside with treatment. At this time, the diagnosis of adult onset still’s disease was thought due to presence of major and minor criteria as prescribed in yamaguchi criteria[5] and injection Methylprednisolone (1gm) was started given through intravenous route once daily for 3 days and subsequently fever subsided. Then tab prednisolone (40mg) 1 tab once daily
after breakfast and Tab Methotrexate (7.5 mg) once in a week was given. Now patient was absolutely fine with this treatment regimen and was discharged in afebrile condition and followed up in OPD after 7-10 days. In the subsequent follow up patient was absolutely fine.

**Discussion:**

In this case our first impression was sepsis in an immunocompromised previously diagnosed dermatomyositis patient due to presence of high grade fever, tachycardia, tachypnaea, sore throat, hepatosplenomegaly, high leucocyte count but in the later part of the story we found that evanescent rash appeared and there were supportive evidences of non infective cause of fever were present and we found high serum ferritin level in the background of ANA and RA factor negative. His CRP was positive and CPK was 80. By seeing this kind of picture we confirmed the diagnosis of AOSD. This was a rare presentation of AOSD in a already proved Dermatomyositis patient.

Adult onset Still’s disease is a rare systemic inflammatory disease of unknown aetiology characterised by quotidian or double quotidian high grade fever, evanescent rash, arthritis and multi organ involvement. It owes its name to George Still who published in 1897 his monograph. On a form of chronic joint disease in children.

AOSD is rare, not readily diagnosed and currently there is no consensus on its incidence and prevalence among different population. Based on the larger review from 1980s it appears that it is slightly more prevalent in women than men and it affects significantly younger population mostly in the age between 16 and 35 years of age.

The aetiology of AOSD, like most Rheumatic disease is unknown. But more recently it has been suggested that alteration in cytokine production have an important pathophysiological role in AOSD\(^{[3]}\). There is increased production of IL2, IFN gamma and TNF alpha seen in AOSD.
AOSD typically manifests as triad of symptoms that include high spiking fever, Evanescent rash and arthritis or arthralgia. Diagnosis remains a clinical one made by Yamaguchi criteria\(^5\). Unlike other systemic Rheumatic disease, it is not associated with Rheumatoid factor and ANA positivity. ESR is raised in all the patient\(^4\) and CRP may be raised. Total leucocyte count is markedly high (Neutrophil predominant). Serum Ferritin level also markedly high ranging from 4000ng/ml to 30000 ng/ml. Treatment of AOSD has centred around the use of NSAIDS, Steroid and anti rheumatoid agent.

**Conclusion:**
AOSD is a rare systemic inflammatory disease of unknown aetiology. Conditions commonly confused with the AOSD are reactive arthritis and other spondyloarthropathies, haemophagocytic syndrome, kikuchi’s syndrome, Sweet’s syndrome, granulomatous disease and dermatomyositis. But in my case report I want to highlight that AOSD can present in a previously diagnosed case of dermatomyositis. The association of AOSD and Dermatomyositis is a rare entity and I have searched all relevant studies but I have not found any case report about the association of AOSD with Dermatomyositis. My case report supports the association of AOSD with Dermatomyositis.

**References:**


2. Colafrancesco, Serena; Priori, Roberta; Alessandri, Cristiano; Perricone, Carlo; Pendolino, Monica; Picarelli, Giovanna; Valesini, Guido (2012). *International Journal of Inflammation* 2012:


Abstract:
A hemangioma is a vascular tumour, arising from endothelial cells that line the blood vessels, and is characterised by increased no. of normal or abnormal vessels filled with blood. Being the most common tumour of infancy \cite{1}, it usually appears in the first weeks of life and grows rapidly over the first 6 months. Half of all infantile hemangiomas have completed involution by age five, 70% by age seven, and most of the remainder by age twelve \cite{2}. Approximately 30% of hemangiomas are recognised in the newborn nursery. Prevalance is increased in preterm infants. The male: female ratio is 3:1.\cite{3} When evaluating a patient with these type of malformations, one must also look for syndromes associated with vascular malformations like Klippel-Trenaunay-Weber syndrome and Sturge Weber syndrome. Other uncommon forms of vascular malformations like PHACE syndrome (a neurocutaneous syndrome associated with large segmental hemangiomas of the face with one or more of the following-posterior fossa brain malformations, arterial cerebrovascular anomalies, cardiovascular anomalies, eye anomalies, and ventral developmental defects\cite{4}).

A hemangioma on face or tongue is a rather unsightly lesion, which may lead to parents pressurising physicians to deliver definite surgical treatment. However, watchful waiting is now widely accepted as the first step in management of non-problematic hemangiomas. In most cases, these lesions involute without intervention.

Incidence:
Hemangiomas occur more frequently in
1. females
1. premature infants
1. white infants
They occur in 1-2.6% of neonates at birth across all races, according to one series\cite{5}.

Etiology:
Hemangiomas usually result from developmental errors that occur at 4-10 weeks gestation. Most cases are sporadic, however they may be

\cite{1}Prof. & HOD Dept. of Gen. Medicine, RKMSP, VIMS; \cite{2}MD, PGT 1st Year, Dept. of Gen. Medicine, RKMSP, VIMS
inherited in an autosomal dominant pattern\textsuperscript{[6]}. Port wine stains are associated with Klippel-Trenaunay-Weber and Sturge Weber syndromes. Mutations in RASA 1 gene have also been implicated\textsuperscript{[7]}.

Hemangiomas usually occur from abnormal angiogenesis that lead to overproliferation of vascular entities. Many angiogenic markers like FGF, VEGF, E-selectin, type IV collagenase are increased during the proliferative phase\textsuperscript{[8]}. During involution, a subsequent decrease in angiogenic factors occur.

Recent studies have discovered hemangioma specific antigens like GLUT 1, merosin, Lewis Y antigen.

**Classification:**

Hemangioma are of three types based on the type of vessel involved. They are:

1. Capillary Hemangioma
2. Cavernous Hemangioma (also called Venous Hemangioma)
3. Plexiform Hemangioma (also called Arterial Hemangioma)

Hemangiomas may be classified by their depth in the skin, number or location in the body. Many hemangiomas consist entirely of a cutaneous component and will present clinically as a bright red non-compressible papule, nodule or plaque when fully developed. These cutaneous or superficial hemangiomas represent 50-60\% of all hemangiomas and can resemble a strawberry when mature.

Hemangiomas can develop subcutaneously without a cutaneous component. When this occurs the hemangioma is described as a subcutaneous or deep hemangioma.

Field hemangiomas are those hemangiomas that cover a large area and begin as multiple erythematous macules that rapidly enlarge and coalesce.

Mulliken and Glowacki in 1982 proposed a biologic classification of vascular tumors and malformations that has gained wide acceptance. They used the following criteria to divide vascular malformations into 2 categories.

1. Vascular tumors, which are known as hemangiomas.
2. Vascular malformations, which are subdivided into high flow (arterial) and slow flow (venous) malformations.

**Capillary Hemangioma:**

Occur mainly in head and neck region.

One of the most common benign orbital tumours of infancy.

Typically absent at birth, rapid growth in infancy with spontaneous involution later in life.

Patient usually presents with a superonasal eyelid or brow lesion with ptosis of the involved eyelid.

**Cavernous Hemangioma:**

Most common intraorbital tumors found in adults.

Manifest as a painless progressively proptotic eye.

Mostly unilateral, but bilateral may be found. Visual acuity compromise, diplopia, or papillary dysfunction can occur from compression of intraorbital contents.

**Signs and Symptoms:**

Hemangiomas are most commonly located in head and neck region, followed by trunk, lower extremities and upper extremities\textsuperscript{[8]}.
The appearance varies from a hypopigmented macule to a bruise-like macule. It grows slowly and gradually through the postnatal months, then involves over 2-6 years. Involution is normally complete within 7-10 years.

Sometimes they grow in internal organs such as the liver, larynx or small and large intestine.

Some are formed during gestation and are called congenital hemangiomas.

The most common (infantile hemangiomas) appear during the first few weeks of life. Infantile hemangioma is often initially misdiagnosed as a scratch or bruise; but the correct diagnosis becomes obvious with further growth.

Multiple hemangioma (hemangiomatosis) appear as multiple smaller lesions.

A subungual hemangioma may present with pseudo-clubbing.

Family history should be thoroughly elicited. Infantile hemangioma may be the part of an autosomal dominant trait.

Being a part of a syndrome complex, other features of Klippel-Trenaunay-Weber syndrome (vascular tumours, varicose veins, soft tissue tumors of extremities) or Sturge Weber (facial hemangioma, epilepsy, seizures, hemiplegia, visual field defects and glaucoma).

**Diagnosis:**

**History**

**Imaging:** MRI- provides exact location + presence of associated neurological abnormalities.

USG- cost effective option.

Prenatal diagnosis of a congenital hemangioma can be done using prenatal imaging.

Biopsy can be performed if malignancy is suspected.

Complications:

In some cases, hemangioma can be life threatening, interfering with breathing, vision, or hearing.

A vascular tumour in upper eyelid can lead to amblyopia.

Visceral hemangiomas can often lead to symptoms. Liver hemangioma may present with jaundice.

GI hemangiomas may present with GI bleed. A respiratory tract hemangioma can cause stridor.

Infants with hemangiomatosis must be evaluated to exclude other internal lesions.

**Management:**

The majority of hemangiomas never need any form of treatment. Some parents feel that hemangioma treatment is necessary because the marks can be disfiguring and may cause social or psychological problems.

Medical intervention may be needed if hemangiomas are located in areas that restrict normal activities or cause severe pain.

Systemic glucocorticoids are the first line therapy. Best effective if administered during
proliferative phase. High success rates have been described at prednisolone equivalent doses of 2.9 mg/kg.6

l Among oral agents, beta blockers are useful, though risk: benefit ratio of their use must be considered. Topical beta blocker timolol lotion may be effective.

l Intralesional triamcinolone injections administered every 4-6 weeks is useful for small hemangiomas.

l Interferon alfa-2a is used for life threatening or deforming lesions that do not respond to glucocorticoid therapy. Subcutaneous dose is 1-3 million U/m² of BSA.

l Recent studies show possible benefit of flashlamp pumped PDL in superficial residual lesions. PDL or argon laser is also the treatment of choice in infants or children with capillary hemangioma. The argon laser is currently used in adults with darker or raised portwine stains.

Surgical Treatment:

Regarding surgical intervention, one must adjust the pros and cons before resecting a hemangioma; whether the result of a surgery would be cosmetically more acceptable than that from medical treatment or not. Some surgeons advocate postponing excision until after the involutional phase of hemangiomas. Scar length with a circular incision would be shorter than that with a lenticular incision.

Prognosis:

As mentioned before, most hemangiomas involute without intervention. Ulceration secondary to infection or trauma may increase the risk of residual scarring. A large facial lesion is most likely to leave an unacceptable scar. The PDL has vastly enhanced the treatment efficacy of cutaneous capillary malformations.

References:


Pictorial Quiz : 1

IDENTIFY THE CASE AND ITS RELATIONSHIP WITH SMOKING

For Answer : See Page 70

Courtesy :
Dr. Jayanta Chakraborty
Prof. & HOD, Dept. of Gen. Medicine, RKMSP, VIMS
IDENTIFY THE INSTRUMENT

For Answer: See Page 70

Courtesy:
Dr. Debasish Maji
Prof., Dept. of Gen. Medicine, RKMSP, VIMS
An electronic cigarette (e-cig or e-cigarette), is a battery-powered vaporizer which has a similar feel to tobacco smoking. Electronic cigarettes do not contain tobacco, although they do use nicotine from tobacco plants. They do not produce cigarette smoke but rather an aerosol, which is frequently but inaccurately referred to as vapor. In general, they have a heating element that atomizes a liquid solution known as e-liquid. E-liquids are usually a mixture of propylene glycol, glycerin, nicotine, and flavorings. Others have similar ingredients but without nicotine.

The benefits and risks of electronic cigarette use are uncertain.

Answer : Pictorial Quiz 1
Smokers suffer more severe GRAVE’S ORBITOPATHY. Smoking increases the likelihood of progression of Grave’s orbitopathy. Quitting smoking is associated with better outcome of different modes of management of Grave’s orbitopathy.

Achievements of Dr. Amal Kr. Chakravarty in 2014

IAPS Conference 2014 at “OOTY”
40th National Conference Oct. 9 -12
A Stellar Education Program featuring the latest advances in the field of Paediatric Surgery.

Paper on Basic Research.

Title: The pathophysiology of perianal soiling and incontinence in high and intermediate Anorectal malformations following surgery.

Authors: Prof. Amal Kr. Chakravarty & Prof. Subir Kr. Chatterjee.

Paper presented by Prof. Amal Kr. Chakravarty.

Dr. Chakravarty was also a chairperson on a session on Paediatric Onco Surgery.

The surgery of imperforate anus is to restore the physiological function of defecation using modern technology and the experience of pioneers. However the problem of perianal soiling remains. The author discussed the anatomical basis of perianal soiling and incontinence.
We express deep sorrow at the passing away of —

**DR. PROMODE BEHARI DUTTA**, MBBS, MS, who was attached to the Department of Opthalmology in this institute from November, 1963 to December, 2014 in different capacities, the last being an Hony, Consultant, passed away on 20th December, 2014.

We remember with respectful gratitude the dedicated and selfless services rendered by him during his long association with this Institute.

We wholeheartedly pray to the Almighty for the eternal peace of the departed soul.

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Journal of the Vivekananda Institute of Medical Sciences