



**Chettinad**  
Health City

**MEDICAL JOURNAL**

International Peer Reviewed Journal



## **CHETMEDICON - 2019**

### **Special Issue**



### **In this issue**

- Mortality In Critically Ill Patients – A Short Review
- Metabolic Acidosis in Critically Ill Patients
- Endocrinopathies – A Trouble Maker In Critically Ill Patients
- Atrial Fibrillation In Critically Ill Patients
- Blood Product Transfusions In Critically Ill Patients
- Pages of History - The 200 years journey of Stethoscope
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**CHETMEDICON 2019**

6<sup>th</sup> Annual Conference



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# Chettinad Health City

## MEDICAL JOURNAL

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## Editorial

Vanakkam

I am very happy to be the section editor of this special edition of our journal released on the occasion of the sixth annual conference CHETMEDICON-2019 conducted by the General medicine department of Chettinad Hospital and Research Institute. The theme of this year's conference is Recent Advances in the Medical Intensive Care Units (MICU). In addition to the lecture series in the conference we have selected certain important review articles which may enrich and update our collective knowledge in the management of critically ill patients.

Though the concept of ICU was given shape in 1953, they were not given much importance initially. By late sixties and early seventies they gradually gained importance and now have become a significant and integral part of medical care. The evolution of ICUs in terms of facilities and equipment has positively influenced the mortality and morbidity rate. In the article 'Mortality in Critically Ill Patients' the authors have noted that apart from the ICU design and type of medical care, the individual patient factors are also important in predicting the mortality in ICUs. The article also elucidates the various mortality predictor scores and how the mortality rate has been improving with various guidelines.

In Medical intensive care unit (MICU) the acid base disorders are the most common metabolic challenges the physicians come across. Metabolic acidosis occurring in MICU are not a simple acid base disturbance but complicated, multifactorial and mixed acid base disorders that are most difficult to tackle. In their review article 'Metabolic Acidosis in ICU setting the authors has detailed the diagnosis and management of various types of acidosis. Authors have also stressed the fact that management of acid base disturbance is not just treating the acidosis or alkalosis but addressing their etiology.

Endocrinal disorders in MICU may be the cause or the effect of various metabolic disorders that a physician comes across in emergency setup. The most common condition all of us are aware is Non thyroidal illness syndrome (Sick Euthyroid syndrome). There are other acute syndromes such as acute adrenal insufficiency, pituitary apoplexy which may not be very obvious mimicking other systemic illness. Unless the treating physicians are alert, these conditions may lead on to serious consequences. In the article Endocrinopathies – 'A Trouble Maker in ICU' the authors have discussed the common endocrinopathies and their management.

Atrial fibrillation (AF) is the most common arrhythmia which a practicing physician comes across. One should not view it as only a primary cardiac rhythm disorder since it actually reflects internal milieu of the patient. Abnormalities in electrolytes, acid base, hypoxia, infection, dehydration, toxins, drugs and trauma are few in the list of factors that can precipitate or aggravate AF. The above mentioned lists are found in the critically ill patients and hence they are prone to AF and its complications. The authors of 'Atrial fibrillations in critically ill patients' discuss the causes and the treatment strategies of atrial fibrillation in MICU.

The critically ill patients are always at the risk of hematological abnormalities, the Commonest being coagulopathies due to thrombotic or bleeding disorders secondary to organ failures or drug induced hematological abnormalities, and sepsis with disseminated intravascular coagulation. In addition, most of these patients may have primary or secondary anemia. Unless it is promptly recognized and managed, it may lead to 100% mortality. Immediate and essential actions that play a critical role in saving the patients are - replacement of loss of RBC, thrombocytes, Fresh frozen plasma, or coagulation factors. The authors in their article highlight the indication and thresholds of various blood products in critically ill patients.

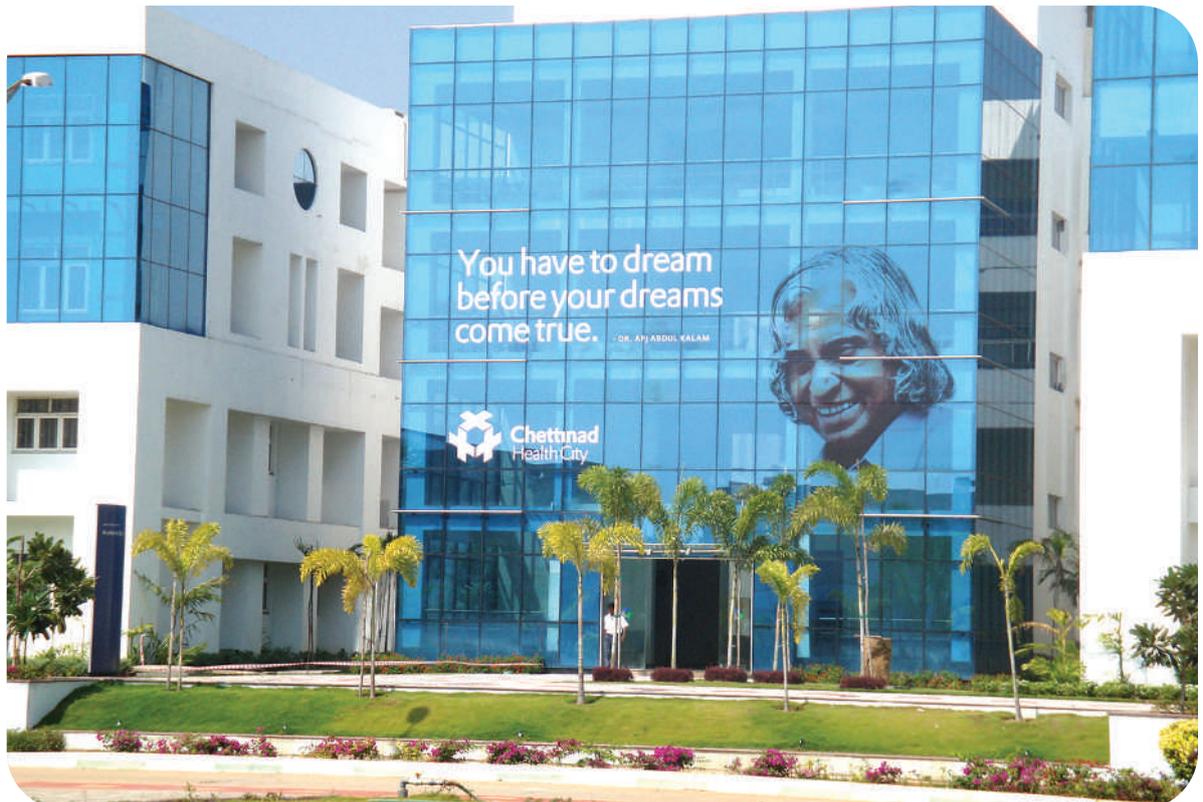
In addition to the review articles, this issue carries the abstracts of the free posters and papers presented in the CHETMEDICON 2019. Hope this issue will be useful to the physicians involved in handling the critically ill patients. I thank Editor Prof. N. Pandiyan and his team for giving me an opportunity to be the section editor of this issue.

யாதானும் நாடாமால் ஊராமால் என்னொருவன்  
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(For the learned, every nation is their nation; and every place is their place; why then, does one shun learning till death.)

## NANDRI

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# Review Article

## Mortality In Critically Ill Patients – A Short Review

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### Abstract

Intensive care units are an integral part of any hospital which deals with critically ill patients who are at extremes of physiological dysfunction. Mortality in critically ill patients vary from 18% up to 40% in various studies across the world due to varied clinical practice, ICU design and individual patient factors. Mortality prediction models such as APACHE score and SOFA score and other scoring tools are used commonly in ICU to prognostic patients and to predict mortality but none of the tools have been shown to be superior among various studies conducted. Demographic factors such level of sophistication of ICU, financial status can adversely affect the prognosis of patients and they are especially important in developing countries such as India. Individual clinical characteristics such as patient's pre-morbid status and co-morbidities, presence of sepsis with shock, acute respiratory distress syndrome have significant effects on the prognosis of critically ill patients. Sepsis is one of the most common disease condition in an ICU setting, although there are limitations to surviving sepsis guidelines, the recommendations are still widely followed in many hospitals. Our understanding of mechanical ventilation has improved tremendously in the past few years with immense data from evidence based studies which has contributed to the decline in ICU mortality and overall hospital mortality.

**Keywords :** ICU mortality, APACHE score, Sepsis, ARDS

### Introduction

Intensive care units are specialized treatment units which provides highly specialized medical care for life threatening organ failures which may develop in acute and chronic diseases at any point during the course of the disease. ICUs provide specially designed monitoring with highly skilled personnel for patients at extremes of physiological deterioration. The concept of critical care unit was introduced in the early 19<sup>th</sup> century by Dr. Walter E Dandy when the exceptional idea of intensive care beds was introduced in Johns Hopkins Hospital in Baltimore.<sup>1</sup>

The notion of intensive care units in India has developed rapidly in the past few decades. Numerous studies have evaluated factors which may predict positive and negative outcomes in critically ill patients but due to the varied nature of critical care units which are markedly different in design, resources, management and care delivery there is no consensus regarding the optimal ICU care. In this review article we will look at some of the factors which contribute to the prognosis of patients who are admitted in an intensive care setting.

### Mortality Prediction Models in ICU

Mortality prediction models have been developed to assess objectively and quantitatively the level of organ dysfunction and predict mortality in ICU patients.

Clinicians and researchers have always known how important performance of ICU is to overall hospital mortality.

Most widely used Mortality predictions models are:-

**APACHE II** – Acute Physiology, Age, Chronic Health Evaluation score The APACHE score was introduced in 1981 by Knaus et.al and an updated version, APACHE II score in 1985, which is the most widely used prediction model for critically ill patients.<sup>2,3</sup> Although APACHE III and IV models have also been in use for a few years now, APACHE II still remains the most widely used when compared to the older and newer models.

Mortality prediction models may not change the clinical management of patients but they are still used in prognosticating patients and may help family members make informed decision about the aggressiveness of care. They are also useful to compare baseline status of patients in clinical trials and studies conducted in an ICU setting, evaluate the success of new or differing forms of therapies.

The APACHE II score uses 12 physiologic measurements, age and previous health status and the score is calculated within first 24 hours of admission to ICU using the initial values or the worst measurement in the first day of admission.<sup>4</sup> The scores range from 0 to 71 and higher scores correspond to increased risk of death and severe disease.

APACHE II Score	Nonoperative	Postoperative
0-4	4%	1%
5-9	8%	3%
10-14	15%	7%
15-19	25%	12%
20-24	40%	30%
25-29	55%	35%
30-34	73%	73%
>34	85%	88%

Table 1 : APACHE scores with corresponding in-hospital mortality rates (adapted from Knaus et.al. 1985)

### SAPS III – Simplified Acute Physiology Score

The SAPS III is an extensive tool which uses 29 parameters to predict mortality in hospitalized patients. Although developed to assess mortality it can also be used to compare mortality across different time and different hospitals.

### SOFA – Sequential Organ Failure Assessment score

SOFA score is one of most commonly used scoring tools used in the ICU settings. The scoring is done at admission and then re-calculated on subsequent days. The mortality rate is nearly 50% with increasing SOFA score and less than 27% when the scores remain unchanged.<sup>5</sup>

The components of the score is divided into six categories, one for each major organ system (respiratory, cardiovascular, hepatic, coagulation, renal and neurological).

SOFA Score	Mortality if initial score	Mortality if highest score
0-1	0.0%	0.0%
2-3	6.4%	1.5%
4-5	20.2%	6.7%
6-7	21.5%	18.2%
8-9	33.3%	26.3%
10-11	50.0%	45.8%
12-14	95.2%	80.0%
>14	95.2%	89.7%

Table 2 : SOFA score and Mortality scores

The table above shows the risk of mortality associated with increasing SOFA scores calculated on admission (initial scores) as well as mortality associated with highest SOFA scores during ICU stay.<sup>6</sup>

### Demographic and Clinical characteristics of ICU patients

Patients who are admitted to intensive care units have significantly severe disease when compared to

patients who are admitted to the ward. Hence, when predicting mortality for a patient, the patient's clinical characteristics and level of sophistication of the ICU plays a very important role.

In a study which was done across 124 ICUs in India, patients who were admitted to ICUs which were well equipped (well equipped ICUs were defined as ICU or hospitals which had Dialysis, CT scan, microbiology, biochemistry and hematology laboratories, echocardiography and cardiac catheterization lab) had a lower mortality when compared to ill-equipped ICUs. (21% vs 28 %;  $p < 0.001$ ). The study also showed that nearly 30% of the ICUs in India were not adequately equipped to handle critically ill patients.<sup>4</sup>

Patients who were admitted to Medical ICU also had higher mortality when compared surgical ICU (medical vs surgical : 20% vs 9%;  $p < 0.001$ ), with higher mortality among patients who underwent emergency surgical procedures when compared to elective ones.<sup>2</sup>

Another entity which contributed to patient mortality was patient's financial source. In India, patients still do not have sufficient insurance coverage or government aid to cover medical expenses. The study showed that 80% of the intensive care patient were self-paying and they had a higher mortality (self paying vs others: 19% vs 16 %).<sup>4</sup> Although it will be difficult to draw conclusions from the above result, the study shows the poor coverage of medical insurance in such a vast country and the need to improve government aid and health insurance to remove economic and financial burden from families and individuals.

Intensive care unit patients are often in severe physiological dysfunction with one or more organ failures. Numerous studies have shown patient's clinical characteristics have a profound effect on the outcome of the patient. Pre-existing illnesses worsen the chances of survival. In a study done in India, presence of co-morbidities (namely Chronic obstructive pulmonary disease, hematological or solid organ malignancies, chronic renal failure, liver failure or immunosuppressive treatment) significantly worsened the mortality in ICU patients. Mortality worsened with increasing number of co-morbidities which can be seen in the table below. Mortality nearly doubles with increasing number of co-morbidities when compared to patients with no co-morbidities.<sup>4</sup>

Number of co-morbidities	All patients	Survivors	Non-survivors	Mortality (%)
0	2536	2147	389	15%
1	1182	923	259	28%
2	268	206	62	23%
3	47	29	18	38%

Table 3 : Mortality associated with Number of co-morbidities

Leading causes of mortality in an intensive care setting are sepsis, cardiovascular failure and respiratory failure. Recognition and prompt initiation of supportive management in the form of administering antibiotics, inotropic support and mechanical ventilation has been shown to reduce morbidity and mortality in all forms of critically ill patients.<sup>7</sup>

ICU patients can develop sepsis which they may have acquired from the community or from the hospital/ICU itself. Severe sepsis or septic shock (defined by Surviving Sepsis Campaign (SSC)) during ICU stay has increased mortality irrespective of other parameters. (OR : 1.699; CI :1.3 – 2.1).<sup>4</sup> Hence prompt recognition of sepsis at the earliest along with resuscitation of the patient according to protocols laid done by Surviving sepsis campaign bear utmost importance.<sup>8</sup> (Sepsis bundles of SSC will be discussed in the following section – Interventions in ICU).

Apart from sepsis and septic shock, patients who have developed acute respiratory distress syndrome (ARDS), as defined by the Berlin criteria (PaO<sub>2</sub>/FiO<sub>2</sub> < 300), have nearly twice the risk of mortality when compared to others who do not have ARDS. (OR : 2.2 ; CI : 1.7 – 2.9).<sup>2</sup> Patients diagnosed to have ARDS require ventilator support, either as non-invasive ventilation or invasive mechanical ventilation and mechanical ventilation was independent predictor of mortality with the most probability for death (OR : 2.8; CI 2.3 – 3.4).<sup>4</sup>

### Interventions in Intensive Care Units

Interventions performed in the ICU for critically ill patients can be to treat a disease, used as substitute for physiological function or can be to tackle a failing organ system in a patient with multi-organ dysfunction.

Infections are one of the most difficult entities encountered in an intensive care setting and they can vary from patients presenting with features of sepsis or SIRS to patients with profound septic shock.<sup>9</sup> Surviving sepsis campaign bundles were initially proposed to achieve targets in patients who presented with features of septic shock within 6 hours (resuscitation) of presentation and within 24 hours (management) of presentation.<sup>10,11</sup>

However, the recent update in the SSC has strong recommendation for specific targets to be achieved within 1 hour of identification of septic shock (Although not all the targets may be achieved within 1 hour but they should be initiated).

The SSC recommends early recognition of septic shock and initiation of empiric broad spectrum antibiotics within first 1 hour of presentation, following the reports from a study done by Rivers et al.<sup>10</sup> Every hour of delay increases the mortality by 7.6%. SSC also recommends at least 2 sets of blood culture before starting antibiotics and a target mean arterial blood pressure above 65 mmHg

with fluid resuscitation or with use of vasopressors.

Recent trials, such as Protocolized Care for Early Septic Shock (ProCESS)<sup>13</sup> trial in the United States, the Australian Resuscitation in Sepsis Evaluation (ARISE)<sup>14</sup> trial and the Protocolised Management of Sepsis (ProMISe)<sup>15</sup> trial in England debunked the earlier recommendations of the SSC and did not show any significant change in mortality or need for organ support in any of the patients although most expert physicians will agree that in management of patients with septic shock SSC guidelines play a vital role.

Surviving Sepsis bundles Resuscitation bundle - 1 hour bundle	Target patients
Measure lactate	All patients
Re-measure Lactate	If initial lactate was elevated (>2 mmol/L)
Blood culture before antibiotics	All patients
Broad spectrum antibiotics within 3 hours for ED admissions and 1 hour for others	All patients
Fluids - 30ml/kg of crystalloids	Hypotension or Lactate > 4 mmol/L
Mean arterial pressure > 65 mmHg	Septic shock or lactate >= 4mmol/L

Table 4 : Surviving Sepsis Guidelines

Mechanical ventilation is one of the defining intervention in an intensive care setting and remains the cornerstone for patients with acute respiratory distress syndrome. Several studies have showed improvement in mortality in ICU patients with increasing evidence based practice of medicine in the critical care setting, with a decrease in crude mortality in 2010 when compared to 1998 (28% vs 31%; OR 0.87 ; CI - 0.8 – 0.94).<sup>16</sup> One of the pioneering trial, The ARDSnet trial, which proposed lower tidal volume (4-6ml/kg) when compared to traditional tidal volume (6-8ml/kg) showed a reduction in mortality from 40% to 31% (p < 0.007).<sup>17</sup> Non-invasive ventilation has also increased over the past few decades which has led to lesser complications associated with invasive ventilation such as ventilator associated pneumonia and ventilator associated lung injury.

Some of other interventions which has improved mortality in critically ill patients are administering

corticosteroids in septic shock patients, intravenous proton pump inhibitors to prevent ventilator associated pneumonia which have changed the outlook of patients who undergo critical care treatment.

## Conclusion

Although the concept of critical care has been a new field of venture in the medical fraternity, evidence based practice has seen tremendous improvements in critically ill patient care over past few decades. Mortality prediction models such as APACHE and SOFA score helps in prognosticating patients in ICU and to follow patient's improvement to medical therapy. Studies done across our Indian subcontinent helps us to realize the need for better equipped critical care units and the need for better funding and financial support for patients and families. Surviving sepsis guidelines have drawn criticism for invasive monitoring such as Central venous pressure and Central venous oxygen saturation monitoring but expert physicians will not deny the need for early recognition of sepsis, prompt administration of antibiotics and maintaining target end points when resuscitating critically ill patients. Mortality in ICU has seen a decreasing trend along with decrease in hospital mortality due to better understanding of the mechanics of invasive and non-invasive ventilation and implementation of strategies to prevent complications in intensive care patients.

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# Review Article

## Metabolic Acidosis in Critically Ill Patients

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### Abstract

Metabolic acidosis is a common finding in ICU patients. Metabolic acidosis in ICU patients is not usually a simple acid base disorder but a mixed acid base disorder. Severe metabolic acidosis is said to be present when pH is < 7.2 and it's found to be associated with very high mortality especially when it occurs rapidly. Clinical Manifestations of severe acidosis are hyperventilation, decreased myocardial contractility, decreased cardiac output, cardiac arrhythmias, systemic vasodilatation, diaphragm dysfunction and CNS depression. For management of metabolic acidosis, understanding its pathophysiology is important. The prognosis of a patient with metabolic acidosis is usually determined by the underlying disorder causing acidosis. Treatment is directed towards the etiological factor causing acidosis and not towards treatment of acidosis. Treating acidosis with intravenous sodium bicarbonate is controversial.

**Key words :** Mixed Acid Base disorders, High Anion Gap Acidosis, Normal Anion Gap Acidosis, Delta Delta Gap, THAM

### Introduction

In this article we will discuss about the following  
 1. Identification of metabolic acidosis  
 2. Difference between simple and mixed acid base disorders  
 3. Classification of metabolic acidosis into High anion gap acidosis and Normal anion gap acidosis  
 4. Meaning of Adjusted Anion Gap,  
 5. Meaning of Delta Delta Gap,  
 6. Causes of Metabolic acidosis in ICU setting and its pathogenesis  
 7. The adverse consequences of metabolic acidosis on the outcomes of the patient and  
 8. Possible ways to correct them.

### Identification of Metabolic acidosis

Though Metabolic acidosis means increase in H<sup>+</sup> ion, the amount of H<sup>+</sup> ion in plasma is very low for routine measurement (around 40 mmol/L). So arterial pH which is 1/ log H<sup>+</sup> measured by ABG is used for diagnosing Acidosis. Metabolic acidosis is present when there is low arterial pH (pH < 7.35) along with low HCO<sub>3</sub><sup>-</sup> (<20 mEq/L). 64% of critically ill patients have acute metabolic acidosis<sup>1</sup>. Severe Metabolic acidosis is said to be present when arterial pH is <7.20.<sup>2</sup>

### Difference between Simple & Mixed Acid Base disorders

In the body, Acid base balance is maintained within a narrow range of 7.35 - 7.45 mainly by Carbonic acid buffering system. When acids accumulate in the body,

H<sup>+</sup> ions increases, HCO<sub>3</sub><sup>-</sup> buffers and neutralises it resulting in production of H<sub>2</sub>CO<sub>3</sub> (Carbonic acid). This H<sub>2</sub>CO<sub>3</sub> dissociates into H<sub>2</sub>O and CO<sub>2</sub> and CO<sub>2</sub> is exhaled thro' lungs. This is how metabolic acidosis gets compensated in the body. This compensatory response occurs within a few hours.

For full compensation of Metabolic acidosis, CO<sub>2</sub> should be exhaled more to make pCO<sub>2</sub> fall by 1.25 mmHg for every 1 mmol/L decrease in HCO<sub>3</sub><sup>-</sup>. If not, compensation is not full and the reason might be a coexistent other organ involvement - for example, a lung condition which will prevent exhalation of CO<sub>2</sub> resulting in persistence of low HCO<sub>3</sub><sup>-</sup> and inappropriately high pCO<sub>2</sub>. This is what is called a Mixed Acid Base disorder. In this example, the type of Mixed Acid Base Disorder is

- Metabolic acidosis with Respiratory acidosis.

There can be other combinations of Mixed acid base disturbance like

- Metabolic acidosis with Respiratory alkalosis
- Metabolic acidosis with Metabolic alkalosis and rarely
- Triple acid base disorder

In ICU patients who generally have Multi organ dysfunction Mixed Acid Base Disorders is more common than Simple Acid Base Disorders.

## Classification of Metabolic acidosis based on Anion Gap (AG)

The next step after confirming the presence of Metabolic acidosis is to use Serum Anion Gap (AG) to differentiate Metabolic acidosis into high AG and normal AG Metabolic acidosis. Serum Anion Gap is a measure of the difference between Unmeasured Anions and Unmeasured Cations in the serum.

$AG = \text{Unmeasured Anions} - \text{Unmeasured Cations}$ .<sup>3</sup> If all Anions (Negatively charged ions) and Cations (Positively charged ions) can be measured, serum Anions and Cations will be equal. But the problem is not all Anions and Cations can be measured. Examples of Unmeasured Anions and Unmeasured Cations are given below.

### Unmeasured Anions

- Albumin
- Inorganic acids like sulphate ( $\text{SO}_4^{2-}$ ), phosphate ( $\text{PO}_4^{3-}$ )
- Organic acids like lactic acid, ketoacids

### Unmeasured Cations

- Potassium ( $\text{K}^+$ )
- Calcium ( $\text{Ca}^{2+}$ )
- Magnesium ( $\text{Mg}^{2+}$ )
- Paraproteins

Generally, Unmeasured Anions are higher than Unmeasured Cations. This means that Measured Cations will be higher than Measured Anions. The formula for calculating Anion Gap is

$$AG = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

Normal AG is  $7 \pm 4$  mmol/L i.e 3 - 11 mmol/L.<sup>3</sup> When Anion gap is higher, Unmeasured Anions are higher and when Anion gap is normal, Unmeasured anions are lesser. High Anion gap acidosis ( $AG > 11$  mmol/L) occurs when there is excess acid accumulation (Unmeasured Anions are mostly Organic acids) which uses up  $\text{HCO}_3^-$  for neutralisation of acidosis. Normal Anion Gap acidosis ( $AG 3-11$  mmol/L) also called Hyperchloremic metabolic acidosis occurs when  $\text{HCO}_3^-$  is lost either from Urine or GIT and there is a counter increase in serum chloride ( $\text{Cl}^-$ ) which gets reabsorbed from the urinary system.

Following are the causes of High anion gap acidosis-

1. Lactic acidosis (accumulation of Lactic acid),
2. Ketoacidosis (accumulation of Ketoacids namely beta-hydroxybutyric acid and acetoacetic acid),
3. Renal Failure (under excretion of normally produced acids) and
4. Poisoning due to Methanol, Ethylene glycol, Propylene glycol or Salicylic acid

Following are the causes of Normal anion gap acidosis -

1. Renal tubular acidosis (RTA)
2. Diarrhoea

3. Infusion of large volume of isotonic saline (accumulation of chloride)
4. Taking carbonic anhydrase inhibitor like acetazolamide (Causes  $\text{HCO}_3^-$  loss in urine) and
5. Patients who have Ureteral diversion like fistula connecting ureter and GIT (Urine  $\text{Cl}^-$  is reabsorbed and urine  $\text{HCO}_3^-$  is not reabsorbed in the gut).

Among the 2 types of Metabolic acidosis, High AG acidosis is more common in ICU.<sup>4</sup>

## Adjusted AG

Once AG is calculated, AG has to be corrected based on serum albumin levels. The formula for Adjusted AG is

- Adjusted AG = Observed AG +  $2.5 * (\text{Normal Albumin} - \text{measured albumin in g/dl})$ .<sup>3</sup>

This is especially true in ICU patients who mostly have low albumin.

## Delta Delta Gap (DD Gap)

This is a formula used in patients with High AG metabolic acidosis to find out whether the high AG metabolic acidosis is a pure high AG metabolic acidosis or whether there is a superimposed Normal AG acidosis or a Metabolic alkalosis on the High AG acidosis. The formula is

- Delta Delta Gap = Delta Anion Gap (D AG)/ Delta  $\text{HCO}_3^-$  ( $\text{DHCO}_3^-$ )
- Also written as Delta Delta Gap = Change in AG/ Change in  $\text{HCO}_3^-$

It's the change in the Anion Gap over the change in  $\text{HCO}_3^-$ . Normally, when acid is produced in the body, there should be a proportionate decrease in the  $\text{HCO}_3^-$ . This is because proportionate amount of  $\text{HCO}_3^-$  gets used up for neutralisation of acid. So change in AG/ change in  $\text{HCO}_3^-$  should normally be around 1. This means there is a Simple Acid Base Disorder which is a High AG Metabolic Acidosis

If Delta Delta Gap is significantly  $< 1$ , it means Combined High AG Metabolic acidosis plus Normal AG acidosis.

- The fall in  $\text{HCO}_3^-$  is disproportionately larger than the rise in AG
- This is possible only when there is an associated normal Anion Gap acidosis

If Delta Delta Gap is significantly  $> 1$ , it means Combined High AG Metabolic acidosis plus Metabolic Alkalosis.

- The fall in  $\text{HCO}_3^-$  is disproportionately lesser than the rise in AG
- This is possible only when there is an associated Metabolic Alkalosis

## High Anion Gap Acidosis in ICU Settings

### Lactic acidosis

Lactic acid is the Organic acid which accumulates in this type of High AG acidosis. This is the commonest cause of High AG acidosis in ICU settings. The normal serum lactate level is 0.5 - 2 mmol/L and it can be measured from arterial or venous sample. Blood lactate levels >4 mmol/L is considered abnormally high. Lactic acidosis can occur due to 2 reasons - 1. Increased Lactate production 2. Decreased clearance of the produced lactate. Increased lactate production occurs when there is decrease supply of O<sub>2</sub> to tissues (hypoxia) or when there is interference with oxidative phosphorylation. This results in anaerobic glycolysis causing increased production of lactate compared to pyruvate. This is seen frequently in ICU patients where patients with shock & sepsis are common.

There are 2 types of Lactic acidosis based on whether Hypoxia also called "Oxygen debt" is the reason. They are

- Type A Lactic Acidosis
- Type B Lactic Acidosis

### Type A Lactic acidosis

Conditions causing it are all forms of Shock, Sepsis, Severe Anemia (Hb<5), Seizures, Vigorous exercise and Rhabdomyolysis (O<sub>2</sub> requirement is more), CO poisoning (due to decreased O<sub>2</sub> delivery to tissues) and Malignancy (tumour tissue hypoxia).

### Type B Lactic acidosis

Here hypoxia is not the reason. This occurs in conditions like Liver failure (impaired clearance of lactate in liver), patients with Thiamine deficiency (this affects Pyruvate Dehydrogenase complex enzyme activity), patients on certain drugs like Metformin, Nucleoside reverse transcriptase inhibitors, Propofol and Linezolid (all these drugs interfere with oxidative phosphorylation), and in poisoning due to Salicylates, Methanol, Ethylene glycol (all these poisons also interfere with oxidative phosphorylation) and due to propylene glycol poisoning.

In ICU settings both Type A and Type B Lactic acidosis are common as there is multiorgan damage and shock.

### Ketoacidosis

Ketoacid is the organic acid which accumulates in this type of High AG acidosis. Examples of Ketoacids are Acetoacetic acid, Beta - hydroxybutyric acid. Ketoacids generally are produced when there is limited glucose availability for tissues. In this setting of low glucose availability, lipolysis occurs in adipose tissue and releases fatty acids. These fatty acids undergo beta -oxidation in liver to form Acetyl - CoA which enters into Krebs' cycle. When Acetyl - CoA production is more, oxidative capacity of Krebs' cycle becomes saturated and the excess Acetyl - CoA

is converted to Ketone bodies. This occurs in starvation, chronic alcoholics and diabetics with severe insulin deficiency (where glucose can't be taken into cells). Doing a blood sugar can differentiate it as Diabetic ketoacidosis and nondiabetic ketoacidosis.

### Diabetic Ketoacidosis (DKA)

In a diabetic, conditions like infection, sepsis, myocardial infarction, pancreatitis, usage of glucocorticoids can precipitate DKA. It is a potentially life threatening condition.

### Starvation Ketoacidosis

This occurs when body stores of glycogen get depleted which usually occurs after 2-3 days of fasting.<sup>5</sup> This is followed by lipolysis of adipose tissues and fatty acids are released and they get converted to Ketone bodies.

### Alcoholic Ketoacidosis (AKA)

This occurs suddenly in Chronic alcoholics who have coexistent liver disease when there is acute ingestion of alcohol or when there is abrupt alcohol withdrawal.<sup>5</sup> NAD depletion is the most important reason for this. Normally, Ethanol is metabolised by Alcohol dehydrogenase to acetaldehyde and then is converted to acetic acid. This process requires NAD (Nicotinamide Adenine Dinucleotide) and during this process NAD gets reduced to NADH (Nicotinamide Adenine Dinucleotide Hydrogenase). This depletion of NAD favours conversion of acetic acid to ketone bodies.

### Poisoning with Ethylene Glycol

Oxalic acid is the organic acid produced when Ethylene glycol poisoning occurs causing High AG acidosis. Ethylene glycol is metabolised in the liver by Alcohol dehydrogenase enzyme. Ethylene glycol poisoning can cause Acute Kidney Injury when oxalic acid combines with calcium to form calcium oxalate which damages renal tubules. This poisoning also causes lactic acidosis because of interference with Oxidative phosphorylation.

### Poisoning with Propylene Glycol

D- lactic acid is the organic acid produced when Propylene glycol is metabolised by Alcohol Dehydrogenase in the liver and this causes high AG acidosis. The Serum Lactate tests generally measure L - Lactate. So serum lactate levels grossly underestimate the level of D- lactate accumulation. Propylene glycol is considered less toxic than Ethylene glycol. It's commonly used as a diluent or drug vehicle for many common intravenous drugs namely lorazepam, diazepam, nitroglycerine, and phenytoin. When these drugs are given in larger doses for more than 2 days, this can accumulate.

### Poisoning with Methanol

Formic acid is the organic acid produced when methanol is metabolised by alcohol dehydrogenase enzyme in the liver. This unmeasured acid is neutralised by HCO<sub>3</sub><sup>-</sup> and as a result serum HCO<sub>3</sub><sup>-</sup> decreases creating a High AG acidosis. It's a common

ingredient in varnish and so it's called wood alcohol. Retina, optic nerve and basal ganglia are highly susceptible to methanol.

## Poisoning with salicylates

Salicylic acid (Acetyl Salicylic Acid - Aspirin) is an organic acid and is unmeasured. It's another example of High Anion Gap acidosis. Acute poisoning occurs when there is ingestion of > 150mg/kg or > 6.5 gm of aspirin. Salicylic acid interferes with oxidative phosphorylation causing anaerobic glycolysis resulting in raised lactic acid and ketoacids.

## Normal Anion Gap Acidosis in ICU setting

Like High AG acidosis, this normal AG acidosis is also commonly seen in ICU patients either as a lone entity or as a combination of High AG acidosis with Normal AG acidosis. It's also called Hyperchloremic Metabolic acidosis.<sup>6</sup> This occurs when HCO<sub>3</sub><sup>-</sup> loss is matched by an equivalent increase in serum chloride concentration. As a result serum anion gap is maintained. There are 3 main reasons for Normal Anion Gap Metabolic acidosis in ICU settings -

1. Conditions where there is excessive base (HCO<sub>3</sub><sup>-</sup>) loss either in Stools (Diarrhoea - cholera ) or in Urine
  - The volume depletion associated with it causes increased reabsorption of chlorides in the renal tubules causing Hyperchloremia thereby maintaining a normal AG
2. Conditions where large volumes of Chloride containing solutions are given like in 0.9% NS resuscitation of hypovolemic shock.
3. Conditions with high AG acidosis like DKA where with fluid replacement Organic acids (which are potential bases) are lost in urine and this is replaced with Normal Saline (NaCl) fluid replacement which increases chloride levels in serum.<sup>6</sup>

This results in the conversion of a High AG acidosis to Normal AG acidosis.

## Clinical Features and Complications of Metabolic acidosis

General Clinical features of metabolic acidosis include hyperventilation (due to respiratory center stimulation in the brain stem), Kussmaul's respiration, confusion, headache, nausea, vomiting, chest pain, palpitations, fatigability, bone pain, hypotension, coma . In DKA breath can have fruity odour. In Salicylic acid poisoning - tinnitus, restlessness, seizures can occur.

Acute metabolic acidosis is associated with Vasodilatation with hypotension, Depression of Cardiac contractility and so depression of cardiac output, Cardiac Arrhythmias and Increased mortality. This is more prominent with high AG acidosis - especially Lactic acidosis than with Normal AG acidosis. This difference might probably reflect the

disorders associated with causing these acidosis and may not be due to the acidosis as such.

## Management of Metabolic Acidosis

### Rx of Etiology

- Generally management of Metabolic acidosis is directed towards the etiology of the Metabolic acidosis

### Lactic Acidosis

- Correction of Hypovolemia
- Antibiotics for Sepsis

### Ketoacidosis

- DKA - Intravenous insulin and Fluid resuscitation
- Starvation and alcoholic ketoacidosis are treated with IV glucose

### Ethylene Glycol & Methanol Poisoning

- Fomepizole (an inhibitor of alcohol dehydrogenase is used)<sup>7</sup>

### Salicylic Acid Poisoning

- Activated Charcoal
- Intravenous HCO<sub>3</sub><sup>-</sup>
- Dialysis

### Treatment & Prevention of Normal AG Acidosis

- This is done using Intravenous balanced salt solution instead of Intravenous chloride containing solutions

### Alkali Therapy

#### IV Bicarbonate

Normally, body compensates for Metabolic acidosis by exhaling pCO<sub>2</sub>. Peak respiratory compensation is said to be present when pCO<sub>2</sub> has fallen to around 15 mmHg. This is usually given when pH is around 7.2. Any further fall in pH can't be compensated by respiration and this further worsens metabolic acidosis.<sup>7</sup>

Generally Intravenous HCO<sub>3</sub><sup>-</sup> is given when pH is < 7.2. to rise the pH to around 7.2. In patients with High AG acidosis like lactic acidosis and DKA, as HCO<sub>3</sub><sup>-</sup> can be generated from these Organic anions, correction with intravenous HCO<sub>3</sub><sup>-</sup> is not done until pH becomes less than 7.0 - 7.1. Amount of HCO<sub>3</sub><sup>-</sup> to be administered is estimated using HCO<sub>3</sub><sup>-</sup> deficit. This is calculated by the formula HCO<sub>3</sub><sup>-</sup> Deficit = (Desired serum HCO<sub>3</sub><sup>-</sup> - Measured HCO<sub>3</sub><sup>-</sup>) \* 0.5 \* body weight<sup>7</sup> To avoid hyperosmolarity and Hypernatremia, NaHCO<sub>3</sub> is given as infusion mixed with 1 liter of 5% dextrose with water. Complications associated with inadvertent use of Intravenous HCO<sub>3</sub><sup>-</sup> are

- Increase in pCO<sub>2</sub>
- The generation of large quantity results in entry of CO<sub>2</sub> into the cell and this can aggravate intracellular acidosis. This complication will be less when tissue perfusion and pulmonary functions are normal
- Fall in ionised Ca<sup>2+</sup>
- Volume overload

- Other Alkali Therapy
  - Sodium Citrate
  - Potassium Citrate
    - This is especially used when there is a combination of metabolic acidosis with hypokalemia
- THAM (Tri Hydroxymethyl Amino Methane)<sup>7</sup>
  - It's a new biologically inert alkali which can buffer CO<sub>2</sub> and acid. It's a more effective buffer than HCO<sub>3</sub> and is well tolerated.

## Conclusion

Analysis of Acid Base disturbance should be done systematically. It's important to classify metabolic acidosis based on Anion Gap. High Anion Gap acidosis is more common in ICU setting. Severe metabolic acidosis (pH <7.2) is associated with higher mortality. Correction of the underlying cause should be the basis for the management of high AG acidosis. Randomised controlled trials in humans are required to evaluate the different approaches towards correction of metabolic acidosis.

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## Identify this !



## A Great Inventor

## A Great Invention



# Review Article

## Endocrinopathies – A Trouble Maker In Critically Ill Patients

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### Abstract

Endocrinopathies may develop in intensive care unit patients and are not uncommon. These disorders pose unique challenges to the attending clinicians as they present non-specifically. Timely diagnosis and appropriate treatment of the endocrine failures can improve the outcome in critically ill patients. In this review article, endocrine disorders involving the thyroid, anterior pituitary and adrenal glands have been discussed.

**Keywords :** Endocrinopathies, Critically Ill, Thyroid storm, Pituitary apoplexy, Adrenal insufficiency

### Introduction

Endocrine emergencies are the common problems encountered by the treating physician in Intensive Care Unit (ICU). These disorders may either pre-exist or develop during the course of hospitalization. Critical illness like myocardial infarction, sepsis, and trauma are characterized by striking alterations in the hypothalamic – pituitary – peripheral hormone axis.

The clinical presentation of the endocrinopathies may be difficult to recognise in ICU especially if the manifestations of the underlying disorder predominate. A high index of suspicion is needed to recognise the endocrine emergencies in critically ill patients, which can significantly influence the outcome and prognosis in these patients. Although, with wider availabilities of newer diagnostic modalities and improvement in treatment that have vastly helped in diagnosing and treating these endocrine emergencies, the morbidity and mortality is still very high due to failure in recognising these disorders early and treating them efficiently. Recognition and safe treatment of several conditions such as acute adrenal insufficiency, thyroid crisis, hypoglycemia and hyperglycemic crisis may be lifesaving.

This review article focuses on important endocrine emergencies involving the thyroid and adrenal glands, which are common in ICU. Emergencies involving the pituitary gland are also included. Hyperglycemic crisis and hypoglycemia which are common in critically ill patients have been extensively discussed elsewhere and it is not covered here because of space limitations.

Other issues that are related to intensive care, such as fluid and electrolyte imbalance like hypocalcemia, hypercalcemia and hyponatremia may have an

underlying endocrine cause and may be treated accordingly with recognition of the disorder; Fluid and electrolyte replacement without correction of the underlying disorder results in insufficient improvement in clinical status of the patient and these disorders are also not discussed here.

### The Thyroid Gland Nonthyroidal Illness Syndrome

It is very difficult to interpret thyroid function test in the ICU because thyroid hormone concentrations are affected by a wide variety of nonthyroidal illness, including sepsis, myocardial infarction, major surgery, and severe malnutrition.<sup>1</sup> In addition, commonly used drugs in ICU including dopamine, corticosteroids, amiodarone, and iodinated radiocontrast agents can also affect thyroid physiology. In the ICU, physicians frequently encounter nonthyroidal illness syndrome (NTIS), previously known as sick euthyroid syndrome.<sup>2</sup> The diagnosis is based on clinical suspicion as well as documenting low serum T<sub>3</sub> levels. In more severe illness, T<sub>4</sub> production also becomes suppressed and the prognosis becomes poor if total T<sub>4</sub> is <4ug/dl. TSH level is typically normal to low.<sup>3</sup>

The mechanisms underlying NTIS are poorly understood, and data on the beneficial effect of thyroid hormone replacement on outcome of the critically ill patients are so far controversial.<sup>4</sup> Similarly, routine thyroid function testing should not be performed without a definite clinical indication in critically ill patients.

Distinguishing primary thyroid disease from NTIS can be difficult in ICU and TSH is the most useful investigation with normal levels excluding primary disease.

Hypothyroid patients should continue their usual thyroxine replacement in the ICU. Thyroid function generally returns to normal as the acute illness resolves.

## Thyroid Storm / Thyrotoxic Crisis

Thyroid storm is a rare and potentially life - threatening state that can occur with untreated or partially treated hyperthyroidism. The precipitating factors for thyroid storm in ICU may include surgery (particularly thyroidectomy), sepsis, myocardial infarction, diabetic ketoacidosis, cerebrovascular disease, trauma, pulmonary thrombo-embolism, or following discontinuation of anti-thyroid medications. The drugs like high doses of iodine-containing compounds (for example, radiographic contrast media), new institution of amiodarone therapy, and salicylates have been implicated in triggering thyroid storm.<sup>5</sup>

Thyroid storm is characterized by an exaggerated response to elevated levels of circulating thyroid hormones. Cardinal features includes fever (>38.5 °C), tachycardia, central nervous system dysfunction (agitation, delirium, psychosis, stupor or coma) and gastrointestinal symptoms (nausea, vomiting, abdominal pain). More severe cardiac

manifestations may include arrhythmias, heart failure and shock.<sup>6</sup> It is very difficult to differentiate the clinical symptomatology of thyroid storm from other medical emergencies such as neuroleptic malignant syndrome, malignant hyperthermia and pheochromocytoma.

Thyroid function tests show suppressed TSH, elevated free T<sub>4</sub> and or T<sub>3</sub>. Other biochemical features include hyperglycaemia, leucocytosis, mild hypercalcaemia, and abnormal liver function tests. Adrenal reserve may be impaired. Blood results cannot discriminate thyroid storm from thyrotoxicosis, as it is a clinical diagnosis.

The aim of treatment includes is summarized in table 1.7

- Treatment of the precipitating events,
- Inhibition of thyroid hormone synthesis and release,
- Reduce conversion of T<sub>4</sub> to T<sub>3</sub>,
- Block the peripheral effects of thyroid hormone,
- Supportive therapy includes IV fluids, cooling blanket, antipyretics such as paracetamol and chlorpromazine for hyperthermia, oxygen therapy, and mechanical ventilation for hypoxemia, fluid and electrolyte replacement, and appropriate management of cardiac arrhythmias and heart failure.

Drug	Mechanism of Action	Dosage
Propranolol	Blocks beta-receptor mediated effect of catecholamines. Reduces peripheral conversion of T <sub>4</sub> to T <sub>3</sub>	0.5 to 1.0 mg IV, every 2 to 3 hours, or 40 to 80 mg, PO, every 4 to 8 hours
Propylthiouracil	Blocks thyroid hormone synthesis and release. Prevents peripheral conversion of T <sub>4</sub> to T <sub>3</sub>	200-400 mg PO or rectally every 4-6hours
Carbimazole	Blocks thyroid hormone synthesis and release	20 mg every 6 hours PO or rectally
Inorganic iodine	Blocks the release of preformed hormone	Lugol's solution - four to eight drops, PO, every 6 hours (1 h after anti-thyroid drug administration)
Hydrocortisone	Blocks peripheral conversion of T <sub>4</sub> to T <sub>3</sub>	300 mg IV stat followed by 100 mg three times a day

Table 1 : Drugs used in treatment of thyroid storm

## Myxedema Coma

Myxedema coma is an uncommon medical emergency that results from undiagnosed, untreated or inadequately treated hypothyroidism with a very high mortality rate (20-60%).<sup>8</sup> This condition is typically seen in obese elderly females. These patients usually present with hypothermia, altered mental status, and an acute precipitating event. Numerous precipitating factors have been identified, including infection especially pneumonia, myocardial infarction, cardiac failure, stroke, trauma, gastrointestinal blood loss and several drugs (e.g. lithium, amiodarone, sedatives, diuretics and anaesthetic agents). Other clinical features include

bradycardia, hypotension, hypoventilation, anorexia, nausea, abdominal pain, and decreased gastrointestinal motility. Clinicians should always consider the possibility of myxedema coma in a patient who presents with a triad of hypothermia, hyponatremia, and hypercapnia with a history of thyroid surgery in the past.

Blood reports frequently show elevated TSH and low free T<sub>4</sub> values. Treatment should be started on the basis of clinical suspicion rather than relying on the investigations and is shown in table 2. Cortisol level should be measured before initiating the treatment, as it may precipitate or unmask the underlying adrenal insufficiency.

Key treatment goals are<sup>9</sup>

- Replacement of thyroid hormones,
- Identification of precipitating factors,
- Supportive therapy includes hemodynamic support with isotonic fluids, passive rewarming techniques, correction of electrolyte abnormalities and
- Administration of hydrocorticoids - 100 mg every eighth hourly

Intravenous T <sub>3</sub>	Initial dose: 10-20 µg First 24 hours: 10 µg q4 h Followed by 1-2 days: 10 µg q6 h
Intravenous or oral T <sub>4</sub>	Initial dose: 500 µg Followed by: 100 µg every day

Table 2 : Replacement of Thyroid Hormones

## Adrenal Gland

### Adrenal Insufficiency (AI)

It is one of the common disorders encountered in critically ill patients. The prevalence of AI varies between 10 to 20% and even rates as high as 60-90% has been reported in patients with severe sepsis.<sup>10</sup>

The adrenal suppression in critically ill patients is often reversible with the treatment of the underlying disorders, and is called critical illness-related corticosteroid insufficiency (CIRCI).<sup>11</sup> The pathophysiology of CIRCI is very complex and may arise as a result of dysfunction of the hypothalamic-pituitary-adrenal axis at any level. As a result of systemic inflammatory response elicited commonly by bacterial toxins, there is failure of adrenal glands to produce adequate amount of cortisol or tissue resistance to the effect of cortisol.

Sepsis is the leading cause of AI in critically ill patients. Others causes include disseminated tuberculosis, HIV and fungal infection, immune adrenalitis, intra adrenal hemorrhage secondary to anticoagulant therapy, Waterhouse-Friderichsen syndrome and metastasis.<sup>12</sup> Drugs that interfere with steroid hormone synthesis and metabolism can also cause AI. Therapeutic glucocorticoid use is also the cause of AI in ICU that becomes clinically apparent when the physiologic stress exceeds the anticipated glucocorticoid requirement.

The symptoms and signs of CIRCI include fever, asthenia, confusion, delirium, coma, nausea, vomiting, intolerance to enteral nutrition associated with hypotension that is refractory to fluid resuscitation and decreased sensitivity to catecholamines. The hallmark of this condition is hypotension that is refractory to volume expansion and responds poorly to vasopressors. The blood biochemistry usually shows hypoglycaemia, hyponatremia, hyperkalemia and metabolic acidosis.<sup>11</sup> A high index of suspicion is needed to recognise adrenal insufficiency in ICU and biochemical diagnosis should not delay treatment.

The diagnosis relies on delta cortisol (change in baseline cortisol at 60 min of < 9 µg/dL) after cosyntropin (250 µg) administration and a random plasma cortisol of < 10 µg/dL in patients with putative symptoms and signs of CIRCI.<sup>11</sup>

Fluids and glucocorticoid replacement are the mainstays of treatment.<sup>12</sup> Current guidelines recommend use of 100 mg of intravenous hydrocortisone after collecting blood for cortisol and adrenocorticotrophic hormone (ACTH) followed by a daily schedule of 300 mg in divided doses. This can be discontinued after satisfactory resolution of the underlying condition.

## The Pituitary Gland

### Pituitary Apoplexy

Pituitary apoplexy is characterized by a sudden onset of headache, visual symptoms, altered mental status, and features of hypopituitarism due to acute hemorrhage or infarction into an existing pituitary adenoma, and rarely in normal pituitary gland.<sup>13</sup> The risk factors include hypertension, major surgery (particularly involving cardiac bypass), anticoagulants, trauma, dynamic pituitary function testing, and various drugs (e.g. oestrogens, bromocriptine, and aspirin).<sup>14</sup> The clinical presentation ranges from relatively mild symptoms to adrenal crisis due to dysfunction of the hypothalamic-pituitary-adrenal axis. If pituitary apoplexy is suspected, hydrocortisone 100 mg intravenously three times a day should be administered without delay and continued until the crisis is over after collecting blood for cortisol, prolactin, follicle stimulating hormone, luteinising hormone, oestradiol (in females), testosterone (in males), free thyroxine, thyroid stimulating hormone, insulin-like growth factor-1, and ACTH. Following stabilization, early neurosurgical opinion should be obtained for surgical decompression and tumour resection as it improves neuro-ophthalmic outcome.

### Diabetes Insipidus (DI)

Central DI (impaired synthesis and release of vasopressin) is commonly encountered in ICU rather than nephrogenic DI (renal insensitivity to circulating vasopressin). It commonly develops in patients following transsphenoidal pituitary surgery, traumatic and hypoxic brain injury, intracranial hypertension, infections like encephalitis and meningitis and brain death.<sup>15</sup> As this disease is characterized by polyuria, patients usually develop dehydration, hypotension and hypernatremia as they are unable to access water. Symptoms of DI may not appear until sodium level exceeds 155-160 mEq/L or serum osmolality exceeds 330 mOsm/kg. Symptoms include confusion, lethargy, coma, and seizures. Criteria to diagnose DI includes urine output >200 ml/hr or 3 ml/kg/hr, urine specific gravity <1.005, urine osmolality <150 mOsm/kg and serum sodium >145 mEq/L after excluding other causes for polyuria in ICU (Diuretics, large resuscitation, mannitol, hyperglycemia and cerebral salt wasting).

Treatment of DI includes<sup>16</sup>

- Calculating and replacing free water loss using  $\frac{1}{2}$  NS; No more than 50% of the water deficit is replaced in the first 24 hours
- Monitoring and replacing urine losses hourly with an appropriate fluid
- If patient is euvolemic, DDAVP can be given. Initial dose is 0.4 to 1 $\mu$ g SC or IV. Subsequent doses titrated according to the urine output and serum sodium
- Monitoring electrolytes at least 4th hourly
- Sodium should not rise or fall greater than 0.5 mEq/h

## Conclusion

Endocrine disorders occurring in ICU patients are common and are often unappreciated in this setting. If left untreated, these disorders are associated with increased morbidity and mortality. Some endocrinopathies like non thyroid illness may not require specific treatment. Thyroid storm, myxedema coma, Addisonian crisis, pituitary apoplexy, and diabetes insipidus can present with nonspecific symptoms. A high index of suspicion is needed to recognise them in ICU especially when the primary disorder is unresponsive to standard therapy. Aggressive management of the patient improves the outcome.

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# Review Article

## Atrial Fibrillation In Critically Ill Patients

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### Abstract

Atrial fibrillation (AF) is a common arrhythmia in critically ill patients and is associated with significant mortality. The pathophysiology of development of AF is multifactorial. Advanced age is the most common risk factor for development of AF. The initial therapeutic strategy should depend on the identification and correction of underlying modifiable risk factor. Unfortunately there are limited data for therapeutic strategies for AF in critically ill patients. Present review summarizes the risk factors, pathophysiology, management of haemodynamically unstable as well as stable patients and anticoagulation therapy in critically ill patients.

**Key Words:** Atrial fibrillation, Critically ill, Mortality.

### Introduction

Atrial fibrillation is a supra ventricular arrhythmia characterized by disorganized atrial depolarization without effective atrial contractions. It is the most common arrhythmia among patients in intensive care units (ICU)<sup>1,2,3</sup> and is associated with worst prognosis and longer ICU stay.<sup>3</sup> Atrial fibrillation can be paroxysmal (terminates spontaneously), persistent (persists beyond seven days) or permanent (if conversion to sinus rhythm cannot be achieved). The incidence of new onset atrial fibrillation in critically ill patients ranges from 5% to 46%.<sup>4</sup> Observational studies done in critically ill patients have identified many epidemiological and disease severity related factors that are associated with development of new onset AF.<sup>5</sup> The increased mortality in AF may be due to its detrimental effect on cardiac output and filling pressures. Thromboembolic complications may further worsen the outcomes.<sup>2</sup> There are limited data on therapeutic strategies for AF in critically ill population in intensive care setting compared to non-critically ill population.<sup>4</sup> This review discusses the predictors and management of atrial fibrillation in ICU.

### Risk factors for Atrial fibrillation

AF can be attributed to many causes and the risk factors vary between general population and ICU patients.<sup>6</sup> Risk factors for development of AF in ICU patients include increasing age, presence of comorbidities, sepsis, renal failure, ICU interventions including vasopressor use, use of pulmonary artery catheters and renal replacement therapy. There is also an increased risk of developing new onset AF with increasing disease severity.

The incidence and prevalence rises with age i.e., 1% if age more than 60 years and 5-15% if age more than 80 years.<sup>1</sup> In case of patient with sepsis, the incidence of new onset atrial fibrillation correlates with that of severity of sepsis.<sup>1</sup> A prospective study done by Rainer M et al showed 7.8% of sepsis patients developed new onset AF and 46% of septic shock patients developed new onset AF.<sup>5</sup>

The incidence reported based on studies range between 27 and 40% and the peak incidence during first 2-4 days.<sup>1,5</sup> Prospective observational study done by Joseph P Mathew et al showed that significant independent predictors of postoperative atrial fibrillation were advanced age, history of atrial fibrillation and withdrawal of Beta blockers and ACE inhibitors. They found reduced incidence of atrial fibrillation in patients treated with beta blockers pre and post operatively.<sup>8</sup> Seguin and colleagues in their study of AF on a surgical ICU reported incidence of new-onset AF of 5.3%.<sup>9</sup> The risk factors associated with development of atrial fibrillation in ICU patients is given in table 1.

Patient factors	Intensive care unit - admission diagnosis	Interventions
Advanced age Obesity Gender - Male Fluid overload Hypotension Hypoxemia Anemia Severity of illness Electrolyte abnormalities Acid-base abnormalities	SIRS Shock Ischemia Cardiac failure Trauma to chest Thoracic surgery	Use of Vasopressor Pulmonary artery catheterisation

Table 1 : Risk factors for the development of atrial fibrillation in Intensive care patients

## Pathophysiology

Studies show that the cause of AF is multifactorial.<sup>9</sup> To understand the various treatment options, some basic pathophysiologic concepts leading to development of atrial fibrillation are discussed below. Research in the recent decades has disclosed an interaction between the initiation triggers and the maintenance factors as mechanism of development of AF.<sup>1</sup> The underlying mechanism for development of AF in older subjects is related to the increased length and dispersion of atrial refractoriness, dampening the recovery of atrial excitability in the older atrium.<sup>6</sup>

In case of sepsis, the exotoxins and endotoxins may contribute to the onset of arrhythmia. Exotoxins like streptolysin or pneumolysin have cardiotoxic potential leading to septic cardiomyopathy whereas endotoxins like lipopolysaccharides of some gram negative bacteria through its Toll-like receptor mediated action may contribute to onset of arrhythmia.<sup>10</sup> AF may be precipitated by elevated levels of circulating proinflammatory cytokines, catecholaminergic stress, electrolyte imbalances, and altered volume status during sepsis.<sup>11</sup> Various studies such as Meierhenrich et al as well as Chung et al found a relationship between elevated levels of CRP and onset of AF suggesting a role of inflammation in initiation and maintenance of AF.<sup>6</sup>

Another subgroup of ICU patients at risk of developing AF are post cardiac surgery patients. Cardiac surgeries involving sutures on the atria induce structural remodelling of the atria resulting in inflammation, myocyte alteration and tissues fibrosis which promote AF. After the onset of AF, there is an electrical remodelling process which involves ion channel function and intracellular calcium homeostasis which leads to shortening of refractory periods of atrial cardiomyocytes. These changes occur within a few minutes and contributes to the persistence of AF. Subsequently, alteration in the intracellular calcium homeostasis, contractile remodelling, dysfunction and further dilatation of atria occurs.<sup>1</sup>

Increased sympathetic tone secondary to operative stress can initiate and sustain atrial automatic potential by lowering atrial refractory period.<sup>6</sup>

In critically ill patients, untreated atrial fibrillation can lead to hypotension, myocardial ischemia, heart failure, shock and organ dysfunction. The mechanism of complications are secondary to loss of atrial contraction and high ventricular rate which in turn leads to impaired ventricular filling.<sup>1</sup>

## Management

Management varies between ICUs, as there are no sufficient data regarding the treatment strategy.<sup>6, 7</sup> Intensivists adapt treatment modality based on their experience. The first priority in management of atrial fibrillation is to identify and to correct modifiable risk factors such as electrolyte

abnormalities, hypoxemia, fluid overload and dehydration that predisposes the patient to develop atrial fibrillation.<sup>4</sup> Management of underlying conditions such as ischemia by revascularization, appropriate antimicrobials for sepsis patients and treating endocrine conditions such as hyperthyroidism are to be done. Adrenergic over stimulation may lead to development of new onset atrial fibrillation. Avoidance or minimisation of adrenergic overstimulation helps in management or resolution. Some of the mechanisms for development of AF and their managements are mentioned in table 2.

Mechanism/Etiology	Management
Myocardial stretch secondary to fluid overload/mitral valve disease	Restriction of fluid, Valvuloplasty
Impaired oxygen delivery to myocardium due to myocardial ischemia, hypovolemia, anaemia	Revascularisation, Fluid resuscitation, Blood transfusion
Electrolyte disturbances such as hypokalemia, hypomagnesemia	Correction of electrolytes according to the goal
Inflammation due to surgery leading to structural remodelling of atria, sepsis	Steroids, Antimicrobial therapy
Adrenergic overstimulation due to inotropic support or stress	Reduction of inotropes, sedation, analgesia, beta blockers
Endocrine disorders such as hyperthyroidism, pheochromocytoma	Betablockers, Thyrostatic drugs, Alpha and beta blockers.

Table 2 : The underlying mechanism and management of Atrial Fibrillation

## Hemodynamically Stable Patient

### Rate Versus Rhythm Control

Factors that favour rate control are (i) age above 65 years (ii) Persistent AF (iii) Fewer symptoms (iv) Hypertension (v) Concomitant coronary artery disease (vi) no history of heart failure (vii) contraindication and unsuitability for cardioversion.

Factors that favour rhythm control are (i) Symptomatic patients (ii) Age less than 65 years (iii) Presenting for the first time with lone AF (iv) no hypertension (v) have congestive heart failure (vi) tachycardia mediated cardiomyopathy and (vi) difficulty in achieving rate control.<sup>4,6</sup>

Rate control can be achieved with drugs like beta blockers, digoxin, calcium channel blockers (diltiazem, verapamil) or amiodarone. Since there are no literature evidence on the optimal pharmacological treatment of AF for ICU patients, the clinician should choose the appropriate agent depending on the potential adverse effect.<sup>1</sup> Each drug group has certain advantages and disadvantages for use in critically ill patients.<sup>12</sup>

Drugs with a low risk profile and short half-life is initially recommended.<sup>1</sup> Beta blockers are mostly used to control rate in AF especially in post myocardial infarction and with stable heart failure cases.<sup>6</sup> Selective beta-1 receptor antagonists slower heart rate (chronotropic), delay conduction in the atrioventricular node (Dromotropic) and reduces myocardial excitability (bathmotropic). Esmolol has very short half-life of 7-10 minutes as it is eliminated by unspecific esterases and hydrolyses and can be given intravenously.<sup>1</sup> Metoprolol was found to be well tolerated in septic shock patients with AF.<sup>10</sup> The adverse effect of beta blocker is that it can potentially worsen haemodynamic status because of negative inotropic activity on myocardium.<sup>1,12</sup>

Digoxin has direct effect on atrioventricular node and may slow down the nodal conduction and reduces heart rate. Digoxin should not be used as first line therapy for rate control due to its slow onset of action.<sup>1,4,12</sup> The benefit of digoxin decreases with adrenergic stress, limiting its efficacy in critically ill patients. Digoxin may be beneficial for patients with heart failure in view of positive inotropic effects. Electrolyte disturbances such as hypokalemia, hypomagnesemia and hyperkalemia exacerbate digoxin toxicity. Digoxin can cause ventricular as well as supra ventricular arrhythmias. The extra cardiac manifestations of digoxin toxicity are blurred vision, flashing lights, nausea, vomiting. In life threatening digoxin toxicity, the administration of digoxin immune Fab is highly effective. In patients with normal kidney function, the plasma half-life ranges from 20-50 hours and in end-stage renal disease upto 4-6 days.<sup>1,12</sup>

Nondihydropyridine calcium channel blockers such as diltiazem and verapamil are used in patients with contraindications for beta blocker. In patients with new onset AF and fast ventricular response, intravenous calcium channel blocker diltiazem found to be more successful. The main adverse effects are increased incidences of hypotension.

Amiodarone has less negative inotropic effects compared to beta-blockers and calcium channel blocker and it is one of the commonly used drug in the ICU setting for the treating atrial fibrillation. The adverse cardiac event most commonly seen is prolonged QT interval while Torsades de pointes can be rarely seen. The common extra cardiac side effects are hypo and hyperthyroidism.

In patients with impaired left ventricular function, digoxin or amiodarone is the pharmacological agent.<sup>13</sup> Multicenter risk index for atrial fibrillation found high incidence of postoperative atrial fibrillation (approximately 32%) and showed episode occurred within first 3 days after CABG and recurrences within 2 days after initial episode. Further it showed administration of amiodarone or digoxin were associated with a lower risk of recurrence.<sup>9</sup> A retrospective study by Liu et al found that beta blockers and amiodarone were most commonly used in new onset AF in sepsis patients followed by non DHP CCB.<sup>14</sup>

Magnesium sulphate has been found to be effective in controlling rate and conversion to normal sinus rhythm.<sup>4</sup> Mechanism of action of magnesium are calcium antagonism, membrane stabilisation and regulation of energy transfer. IV magnesium has high therapeutic index and minimal negative inotropic effects. Prophylactic use of IV magnesium may reduce the occurrence of atrial fibrillation after cardiac surgery.<sup>13</sup> Magnesium sulfate has synergistic effect when combine with digoxin in controlling ventricular rate.<sup>4</sup>

Dronedarone and dofetilide may be useful for cardioversion. Dronedarone is an oral multichannel blocker with reduced lipophilicity and no iodine components when compared to amiodarone. The risk of increased mortality in patients with heart failure and risk of severe hepatotoxicity and nonavailability for IV administration limit its use in ICU settings. Vernakalant targets atrial specific channels and is approved for pharmacological cardioversion of AF of less than 7 days duration. It can be given intravenously. The safety and efficacy data for use in critically ill patients is lacking.<sup>1,12</sup>

A prospective study conducted on septic patients with atrial fibrillation showed that majority reverted to sinus rhythm with either electrical cardioversion or medical therapy with amiodarone, beta-blockers, digitalis glycosides or a combination of these.<sup>9</sup>

Substances	Recommended dose
Esmolol	1.0 mg/kg in boluses of 10–20 mg iv, followed by continuous infusion (start with 0.05 mg/kg/min, increase dose every 30 minutes if necessary)
Diltiazem	0.25 mg/kg iv over 2 minutes, followed by continuous infusion (10–15 mg/h) if necessary
Amiodarone	150–300 mg iv, followed by a continuous infusion (900–1200 mg daily) up to 0.1 g/kg Maintenance dose 200 mg daily
Digoxin	0.25–0.5 mg iv every 4–8 h up to 1 mg, followed by maintenance dose of 0.25 mg daily

Table 3 : Commonly used intravenous antiarrhythmic substances in ICU and the recommended dose.

## Haemodynamically Unstable

In patients with dyspnea, acute chest pain or haemodynamic instability, sinus rhythm must be immediately restored by synchronised electrical cardioversion.<sup>15</sup> The aim is to determine whether the cause of instability is arrhythmia or underlying condition.

The initial management include (i) restoration of adequate perfusion with fluids, vasopressors and / or inotropes depending upon the aetiology, (ii) to ensure patient comfort with sedation and analgesia, (iii) to reduce sympathetic activation and maintaining sufficient oxygen supply to myocardium. Synchronised cardioversion is unlikely to provide benefit if tachycardia is a compensatory mechanism. The success rate is inversely proportional to chest wall impedance, left atrial size and duration of atrial fibrillation. Biphasic waveforms and anterior-posterior electrode placement provide higher success rates than lateral electrode positioning and monophasic waveforms. Due to wound dressing and chest tubes in post cardiac surgery patients, studies recommend single shock of 200 joules to be given to increase success rate in view of high impedance. Based on studies it is proposed that high initial energy reduces the incidence of tachyarrhythmic complications. To restore sinus rhythm in patients with pacemakers or internal cardioverter/ defibrillators (ICD) an internal overdrive pacing and or cardioversion may be attempted by cardiologists.<sup>1</sup>

## Long Term Treatment After Haemodynamic Stabilisation

### Anticoagulation

Presence of AF increases the risk of stroke and thus the priority of long term AF management is prevention of stroke. A retrospective study which evaluated association of atrial fibrillation and hospital mortality in critically ill patients showed 5.5% of incidence of stroke associated with atrial fibrillation. Walkey et al showed that patients with severe sepsis had a six-fold increased risk for in-hospital stroke as compared with hospitalized patients without severe sepsis.<sup>16</sup> The one year thromboembolic stroke and bleeding risk are assessed with CHADS-VASc and HAS-BLED but not validated in ICU populations. Anticoagulation poses a challenge in critically ill due to the potential need for urgent surgery or procedures and risk for coagulopathy.<sup>4</sup> In view of short half-life and reversibility with protamine, unfractionated heparin is the drug of choice for ICU patients. In view of ongoing inflammation and procoagulatory state, the risk is even higher in critically ill patients. Short term anticoagulation is accomplished with unfractionated heparin. After an overlap and INR of target range, heparin is stopped and initiated with oral coumarins for long term anticoagulation. Due to lack of evidence in critically ill patients, newer anticoagulants such as thrombin inhibitors and oral factor Xa inhibitors are not recommended.<sup>1</sup>

### Discussion

Atrial fibrillation is the most common arrhythmia in critically ill patient. The risk factors for development of atrial fibrillation in intensive care unit are old age, use of vasopressors, use of pulmonary artery catheter and disease severity.<sup>2</sup> Severity of illness (APACHE II, SAPS II, shock, SIRS) organ failures and sepsis were all reported risk factors for development of atrial fibrillation.<sup>17</sup>

Atrial fibrillation in critically ill patient is associated with worst prognosis and longer stay in hospital.<sup>3</sup> Though AF is a common arrhythmia and associated high mortality and potential long term consequences, a thorough research on treatment of AF in critically ill patients is lacking. As there are no treatment guidelines, the treatment decision depends on treating clinician's experience. Haemodynamically unstable patients need synchronised cardioversion but the conversion rate in critically ill patients is lower (35%) compared to outpatients (90%). The decision for rate control versus rhythm control in haemodynamically stable patients should be based on various patient factors and underlying conditions. Evidences are lacking to substantiate one approach over the other. Studies show in haemodynamically stable patients, first option being rate control with beta blocker or calcium channel blocker, if beta blockers are contraindicated. In cases refractory to beta blockers or calcium channel blockers, amiodarone should be used. In view of highly variable conversion rates, no pharmacologic strategy was identified as superior to another.<sup>4</sup> Further studies are needed to determine the attributable morbidity and evidence to substantiate optimal therapy. Future research should aim for development of risk prediction tools to favour AF prevention in the ICU and for developing therapeutic strategy in critically ill ICU patient.

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# Review Article

## Blood Product Transfusions In Critically Ill Patients

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### Abstract

The Intensive Care Unit in every hospital consumes a large number and variety of blood products on a daily basis. Although commonly used, there is no consensus on the trigger and outcomes of usage of packed cells, plasma, platelets and other products.

Multiple studies have shown the detrimental effect of the inadvertent use of packed cells, thus cautioning against a low threshold for transfusion in most ICU patients. It has been emphasised that transfusion based on patient related factors such as symptoms of hypoxia, lactic acidosis and heart failure should be utilised rather than an arbitrary haemoglobin value.

Also, prophylactic use of platelets or plasma in non-bleeding patients has been shown to not have any benefit, in addition to causing worse outcomes. This review article focuses on highlighting some evidence based key points related to threshold and indications for various blood product transfusions in the ICU.

**Key Words:** Blood transfusions, ICU- Intensive Care Unit, Anaemia, Coagulopathy.

### Introduction

It has been estimated that nearly fifty percent of patients getting admitted in the intensive care unit require some blood product transfusion during their stay in the hospital.<sup>1</sup> Thirty to 45% receive red cell transfusion,<sup>2</sup> 10–30% receive plasma transfusion and 10–20% receive platelets.<sup>3</sup> However, no single guideline exists for the initiation of such said transfusions, leading to a widespread variability in outcome. Also, the impact of these transfusion on the length of hospital stay and the increase in adverse events have not been established. This article deals with an analytical approach to each blood product transfusion, emphasising on threshold for usage, and possibly, its impact on outcome.

### Red Blood Cell Transfusion

RBC transfusions are the most commonly used blood products in the ICU. It has been well established that RBC transfusions in the setting of acute blood loss are lifesaving.<sup>4</sup> However, in the setting of a long term critically ill patient, RBC transfusions have been shown to be detrimental.<sup>5</sup> The extent of blood loss due to frequent sampling in the ICU has been undermined and is an important cause of anemia in the critical care unit. The tolerance threshold for anemia varies greatly between critical and non-critical patients. Red blood transfusions have

been shown to be detrimental in multiple studies.<sup>6</sup> In acute coronary syndrome, blood transfusions have been shown to have adverse outcomes. However, blood transfusions may be useful for STEMI patients, especially those in the elderly age group.<sup>7</sup> We have most evidence for the transfusion threshold in critically ill from the TRICC (Transfusion Requirements in Critical Care) trial. It showed that patients with a restrictive threshold (Hemoglobin of 7 g%) had a better outcome than patients with a liberal threshold (9 - 10 g%).<sup>8,9</sup> However, it is recommended to have a higher threshold (8 g%) in patients with sepsis and symptoms suggestive of poor tissue perfusion. Hence, a patient centric approach is advisable. The decision to transfuse a patient should be tailored, taking into account several factors, including signs and symptoms of tissue hypoxia (angina pectoris, cognitive dysfunction), increased blood lactate levels or electrocardiographic changes suggestive of myocardial ischemia.<sup>10</sup>

### Plasma Transfusions

Fresh frozen plasma is an active way to provide multiple coagulation factors to a bleeding patient. However, a large number of plasma transfusions are done on non-bleeding patients. There is no proper consensus on the outcome associated with prophylactic plasma transfusion. Furthermore, prophylactic plasma transfusions can cause acute lung injury, leading to increased time on the ventilator.<sup>11</sup>

Although commonly used, the International Normalised Ratio is not an ideal tool to assess the risk of bleeding. In fact, 30% of ICU patients have an INR >1.5. The risk of procedure related bleeding is extremely low even in patients with elevated INR. The risk of major bleed after central venous line insertion has been found to be only 0.1-0.8%, whereas that of minor bleed 2.2-6% in patients with INR>1.5.<sup>12</sup> This raises further questions on the role of prophylactic plasma transfusions. The other issue on hand is the volume of plasma to be transfused. It has been shown in large scale randomised controlled trials that administration of low dose plasma(12mL/kg) produces a similar improvement in the coagulation profile as a high dose of plasma(20mL/kg).<sup>13</sup>

To conclude, use of elevated INR, or other factors such as a drop in systolic blood pressure as a predictor of active bleeding is obsolete. Also, use of plasma should be restricted to patients having active or major bleeding which does not include mucosal bleed. The OASIS criteria defines major bleeding as that causing reduction in hemoglobin of >2g%, intracranial, intraocular or retroperitoneal haemorrhage, or bleeding requiring at least two packed cell transfusions. Also, prophylactic peri procedural plasma transfusion is also not advised as the procedural bleeding risk is negligible. Finally, lower volumes of plasma transfusion are sufficient to protect against bleeding in most clinical situations in the critically ill.

## Platelet Transfusions

Platelets are the third most commonly used blood product in the ICU. They are used in various settings such as blood malignancy, sepsis with coagulopathy, viral haemorrhagic fevers, liver disease associated thrombocytopenia and bone marrow failure. However, the elevation of platelet count post transfusion varies between patients, so as the wide variability in clinical improvement. The thrombocytopenia seen in the ICU is usually multifactorial, induced by a combination of inflammation, infection and coagulopathy in contrast to the chemotherapy induced thrombocytopenia seen in non-critical care patients. Hence, there should be a difference in approach as well.

It was initially believed that single donor platelet transfusions (SDP) are safer as compared to random donor platelet (RDP) transfusion due to the reduced risk of alloimmunization. However, studies have shown that leuko-reduced RDP transfusion has a similar safety profile to SDP transfusions.<sup>14</sup> Also, storage of SDP requires more complicated equipment, hence making RDP more cost efficient, especially in developing countries. Moreover, after 5 days of storage, SDP have been seen to lose their efficacy.

For the purpose of hemostasis, the number of platelets required is quite low. Studies have shown that platelets as low as 5000/cumm are sufficient to maintain endothelial integrity.<sup>15</sup>

Also, it has been observed that above a threshold of 10,000/cumm, increasing platelets iatrogenically has not shown a reduction in the incidence of spontaneous bleeding. This was observed majorly in Dengue patients.<sup>16</sup> Platelets administered can either be apheresis units or blood derived platelets. A standard platelet transfusion is that containing a single apheresis units or blood derived platelets equivalent of  $3 \times 10^{11}$  to  $6 \times 10^{11}$  in number. Any dose double this is considered a high dose platelet transfusion.<sup>17</sup> A standard platelet dose has been shown to elevate the blood platelets by 10,000-19,000 / cumm, whereas that of a high dose transfusion raises platelets by 24 - 38,000 / cumm. However, this increase in platelets has not been seen to have an impact on mortality, with outcomes similar in both groups. Hence, prophylactic transfusion of platelets is not recommended, and must be reserved for those with levels <10,000/cumm or active bleeding manifestations. Random donor platelets are cheaper and more practical for usage in a third world setting.<sup>18</sup>

## Cryoprecipitate Transfusion

Cryoprecipitate is less commonly used, and not easily available as compared to other blood products. It is useful in two major setting- haemophilia and low fibrinogen disorders. There is very little published data on the use of cryoprecipitate in the ICU in low income countries. In most countries, it is licensed for use only in congenital bleeding disorders such as haemophilia and congenital hypofibrinogenemia syndromes. It has also proven to be useful in some patients with Von Willebrand disease.

It would be apt to transfuse cryoprecipitate when the fibrinogen levels are <1g/L, as is commonly practiced in North America and Canada. A disadvantage seen with cryoprecipitate use is if not used within 4 hours of thawing, it loses its efficacy. A standard dose established from various studies is one unit per 5-10kg body weight, which will raise the blood fibrinogen levels by 1g/L. To conclude, the usage of packed cells with plasma in the event of acute blood loss has been well documented. Hence, due to lack of availability of cryoprecipitate, plasma may be administered in the event of an appropriate clinical setting.<sup>19</sup>

## Conclusion

There is no uniform consensus on the use of various blood products in the critical care unit. Also, various studies have established that arbitrary lab values do not reflect on patients' eventual outcome. Hence, it is prudent to choose the type and volume of blood product based on relevant information obtained on the clock, with emphasis on patient centric parameters observed on the bedside, which will have a better impact on patient prognosis.

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# Pages of History

## Paper To Digital... And Still Listening: The 200 Years Journey of Stethoscope

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Chettinad Health City Medical Journal 2019; 8(2): 55



Figure. 1 : An early Laennec stethoscope  
PC. <https://en.wikipedia.org>

The word stethoscope is derived from two Greek words, 'stethos' meaning chest and 'scopos' indicating examination. A French doctor named Rene Theophile Hyacinthe Laennec invented the first stethoscope in 1816. Laennec was born in Quimper, Brittany in 1781. He did medicine in Nantes and then in Paris. He worked as a consulting physician at the Necker Enfants Malades Hospital in Paris where his interest in TB (which he contracted later) made him keenly listen to the chest. During an examination of a young overweight female patient, he thought it was improper to place his ear on her chest. So he attempted to find a way to avoid doing this. He used a rolled sheet of paper to create a tube to facilitate auscultation by placing one end of the tube to her chest and the other end at his ear.<sup>1,2</sup>

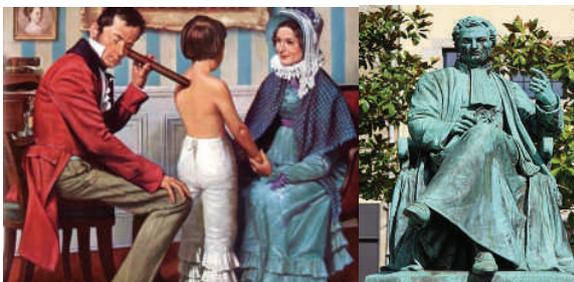


Figure. 2 : Laennec examining with his stethoscope and his statue. PC.- <https://commons.wikimedia.org>

In 1840, Golding Bird designed a stethoscope that had flexible tube and single earpiece. It was not until 1851 when the stethoscope had its next major improvement, which was to make the device bi-aural.<sup>3</sup>

It was invented by Irish physician Arthur Leared, and refined by George Cammann in 1852. In 1858, Somerville Scott Alison described a stethoscope which had two separate bells, allowing the user to hear and compare sounds derived from two discrete locations. In the early 1960s, David Littmann, a Harvard Medical School professor, and cardiologist patented a new stethoscope which had vastly improved acoustical performance. He transformed the stethoscope from a listening device into a powerful diagnostic tool.<sup>4</sup>



Figure. 3 : Electronic stethoscope  
PC. <https://stethoscopes.ninja/best-electronic-stethoscopes>

Throughout the 20th century many minor improvements were made to these iconic devices to reduce weight, improve acoustic quality, and filter out external noise to aid in the process of auscultation. Electronic versions of the stethoscope were introduced to further amplify sounds. Stethoscopes are now available in a wide array of styles, with designs available for virtually every branch of medicine.

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## Abstracts - Oral Papers

### Does PF Ratio Help in Choosing The Mode of Ventilation In ARDS? An Experience from A Tertiary Care Centre

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Chettinad Health City Medical Journal 2019; 8(2): 56

#### Introduction

ARDS is a life-threatening condition with significant impact on the morbidity and mortality of critical care patients. The use of Non-invasive ventilation (NIV) in ARDS is still controversial as NIV failure is associated with worse prognosis. However there is no classification system that facilitates an optimal prognostication of mortality in ARDS patients. This is a prospective study done in Medicine ICU between June 2018 and May 2019 in which the association of PF ratio at admission and NIV failure in ARDS patients who are put on NIV is studied.

#### Materials and Methods

All patients diagnosed to have ARDS according to BERLIN criteria above the age of 18 without any cardiac disease were included in the study. Patient's PaO<sub>2</sub>/FiO<sub>2</sub> ratio (with PEEP ≥5cm of water on NIV) at admission was recorded based on which the patients were stratified into 3 categories as mild, moderate and severe ARDS. The outcome of NIV was studied as to whether the patient had to be put on invasive ventilation due to NIV failure or the patient had improved with NIV during the hospital stay.

#### Results

All patients with PaO<sub>2</sub>/FiO<sub>2</sub> ratio less than 100 on NIV required invasive ventilation subsequently due to NIV failure which is significantly higher than the number of NIV failures among patients in the mild and moderate ARDS category.

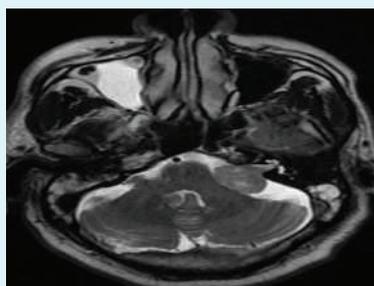
#### Conclusion

In patients with ARDS, the PaO<sub>2</sub>/FiO<sub>2</sub> ratio at admission is a valuable parameter to decide on choosing the right mode of ventilation thereby avoiding NIV failure and redundant long-term invasive mechanical ventilation.

#### Key words

Non Invasive ventilation, ARDS, Mechanical ventilation.

#### Image Challenge - 01



Clue : 50 years male with H/O tinnitus, giddiness, decreased sensation of left side of face

- Answer in page : 64

## Correlation Between Serum Vitamin - D3 Levels and Blood Pressure in Patients with Essential Hypertension and Normotensive Individuals

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Chettinad Health City Medical Journal 2019; 8(2): 57

### Introduction

Vitamin D, a fat-soluble vitamin is produced when ultraviolet rays from sunlight strike the skin. It's seen that lower circulating 25(OH)D levels were associated with higher blood pressures.

### Materials and Methods

An observational study was conducted on 60 individuals in the out patient department of Mahatma Gandhi Medical College and Research Institute between January to December 2018. Based on history and blood pressure values (JNC 7), the population was divided into cases and controls who age and sex matched. Serum Vitamin D levels were measured and classified into deficiency (<20ng/ml), insufficiency (20-30ng/ml) and sufficiency (30-100ng/ml). Statistical analysis was done using independent t test, one way ANOVA and correlation.

### Results

Among the hypertensive individuals, 90% were Vitamin D deficient and 10% had insufficiency. The mean Serum Vitamin D level in essential hypertension was  $14.6 \pm 4.401$  (P value < 0.001). Serum Vitamin D levels were affected significantly by increasing BMI (P value < 0.001) and less sunlight exposure (P value < 0.001) among both cases and controls. There was also a significant negative correlation between serum vitamin D levels and systolic blood pressure (P < 0.001).

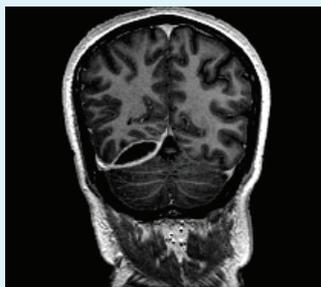
### Conclusion

Isolated systolic hypertension was associated with lower serum Vitamin D levels. Obesity and reduced sunlight exposure were also associated with lower serum Vitamin D levels.

### Key words

Vitamin D3 levels, hypertension, obesity.

### Image Challenge - 02



Clue : H/O right ear pain & discharge since 5 days presents with Fever & Headache

- Answer in page : 65

## A Study on Association Between Red Cell Distribution Width and Glycated Hemoglobin in Diabetes

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Chettinad Health City Medical Journal 2019; 8(2): 58

### Introduction

DM is associated with high morbidity and mortality which makes it a global health problem. Red blood cell distribution width (RDW) is an expression of the variation in size of red blood cells. Recently, RDW has been found to be useful as a prognostic marker in cardiac failure, myocardial infarction and other systemic disorders

### Aims and Objectives

1. To compare RDW with HbA1C level in diabetic patients
2. To establish a correlation between HbA1C level and RDW

### Materials and Methods

A Cross Sectional Study was done in 130 diabetic patients attending Medicine OPD at CHRI. The duration of diabetes and medications taken were recorded with laboratory parameters like CBC, HbA1C and RBS values.

### Results

This cross sectional study was done in 130 diabetic patients of which 79 were male and 51 were female. Majority of the patients were in the age group of 46-65 years. RDW and HbA1C levels were compared and a positive correlation was seen between RDW and HbA1C. Pearson correlation value was 0.882 which was statistically significant at  $p < 0.001$ . RDW level increased with increase in HbA1C level. The study also indicated that higher the value of HbA1C, higher is the RDW value.

### Conclusion

RDW along with HbA1C may be considered as a marker of glycemic control in diabetic individuals as there appears to be a positive correlation between HbA1C and RDW.

### Key words

RDW, HbA1C, Diabetes mellitus.

### Image Challenge - 03



Clue : Left sided hypochondrial pain radiating to left shoulder

- Answer in page : 66

## A Cross Sectional Study to Assess the Diurnal Rhythm of Pulmonary Ventilation in South Indian Population

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Chettinad Health City Medical Journal 2019; 8(2): 59

### Introduction

Despite the known evidences about pulmonary function, discrepancies in diurnal rhythm and ethnicity that prevails in lung function remains to be elucidated. The aim of this study was to determine the magnitude of pulmonary function variability during the usual daytime hours in healthy south Indian population.

### Materials and Methods

Study participants were healthy South Indian volunteers between 18 - 26 years of age. Study participants with bronchial asthma, COPD, acute airway/pulmonary parenchymal infection, systemic or autoimmune disorders were excluded. Smokers and subjects on shift work were excluded. Pulmonary function including PEFR, FEV<sub>1</sub>, FVC & PIFR were assessed on 2 days at 07:00 – 08:00, 09:00 – 10:00, 11:00 – 12:00, 14:00 – 15:00, 16:00 – 17:00 & 18:00 – 19:00 with minimum of 3-day interval using RMS Helios 10 Spirometer.

### Results

The lowest and highest FVC & FEV<sub>1</sub> values were found in the 18:00 – 19:00 and 11:00 - 12:00 time intervals respectively in both the sexes. Lowest airway resistance i.e. the highest PEFR values were observed between 14:00 and 15:00 and the highest airway resistance is recorded between 07:00 and 08:00. Peak Inspiratory Flow Rate was highest between 18:00 – 19:00 pm and lowest in the morning 07:00 – 08:00.

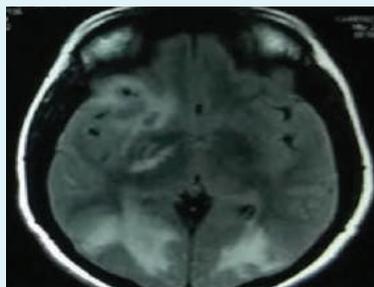
### Conclusion

Airway resistance is found low during the mid-day in healthy south Indian population. Further studies on diurnal variation in pulmonary function, their ability to predict airway disorders and application in therapeutic management of airway disorders must be investigated in future.

### Key words

Pulmonary function, Diurnal rhythm, Airway resistance.

### Image Challenge - 04



Clue : 38 yrs female with headache and blurring of vision

- Answer in page : 67

# A Comparative Study of Clinical and Angiographic Profile of Acute Coronary Syndrome in Young Diabetics and Non-diabetics in a Tertiary Care Centre

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Chettinad Health City Medical Journal 2019; 8(2): 60

## Introduction

The clinical presentation and angiographic findings of CAD varies in diabetic and non-diabetic and also varies with the age of presentation. This study compares the clinical presentation and angiographic changes in patients with the acute coronary syndrome with diabetes and without diabetes below the age of 45 years. Coronary artery disease in patients below the age of 45 is a special subset. The clinical presentation of coronary artery disease in young patients with various risk factors differs, which plays an important role in management strategies.

## Materials and Methods

It is a comparative study in young patients (Age group <45 years) who presented with acute coronary syndrome. Patients were subdivided into two major groups, Group 1 (ACS with DM) and Group 2 (ACS without DM) and analyzed for the clinical and angiographic pattern.

## Results

Pattern of involvement of coronary arteries as assessed by the coronary angiographic study is found to be different in younger CAD patients. Atypical clinical presentation and distinct angiographic finding are common in diabetics below the age of 45.

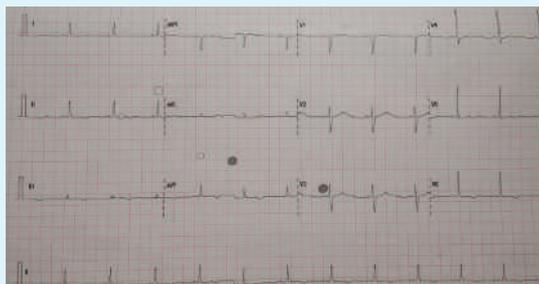
## Conclusion

According to our study SVD is the most common angiographic finding in younger patients presenting with acute coronary syndrome. When comparing diabetics and nondiabetics, diabetic patients had higher proportion of DVD than in non diabetic patients.

## Key words

Acute Coronary Syndrome, Angiography, Diabetes.

### Image Challenge - 05



Clue : Case of post MI Presented with transient VT

- Answer in page : 68

## Assessment of Safety & Efficacy of Bromocriptine in Comparison with Teligliptin in Newly Diagnosed Type 2 Diabetes Mellitus

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Chettinad Health City Medical Journal 2019; 8(2): 61

### Introduction

Bromocriptine and teligliptin were approved for the treatment of type 2 diabetes mellitus in 2009 and 2015 respectively. Though bromocriptine has good safety profile, it is not widely prescribed, whereas the recently introduced teligliptin is widely used. Hence the purpose of this study was to evaluate the efficacy and safety of bromocriptine in comparison with teligliptin in newly diagnosed type 2 diabetes mellitus.

### Materials and Methods

It was a prospective, randomized, open labeled, controlled study done in 50 newly diagnosed type 2 diabetic patients. They were randomly divided into two groups, bromocriptine group (25 patients) and teligliptin group (25 patients). Bromocriptine 0.8 mg was administered in the morning with food from 1st day and increased to 1.6 mg from 15th day and maintained at 1.6 mg till the completion of the study (3 months). Teligliptin 20 mg was administered once a day after food in the morning for 3 months. FBS, PPBS, HbA1c and BMI were assessed at baseline and at the end of 1st, 2nd and 3rd months. Statistical analysis was done using student t test and ANOVA.

### Results

Both bromocriptine and teligliptin significantly reduced FBS, PPBS, HbA1c and BMI values (p value < 0.05). However, teligliptin was found to be superior to bromocriptine in the reduction of FBS and PPBS at the end of 3 months. There was no significant difference between the groups for the reduction in BMI and HbA1c. Teligliptin was well tolerated with no adverse events, whereas 5 patients in bromocriptine group reported nausea.

### Conclusion

Both teligliptin and bromocriptine significantly reduced FBS, PPBS and HbA1c in newly diagnosed type 2 diabetes patients and were well tolerated. Teligliptin was found to be superior to bromocriptine in reducing FBS and PPBS.

### Key words

Teligliptin, Bromocriptine, Type 2 Diabetes Mellitus.

### Image Challenge - 06



Clue : 55 years male with bone pain

- Answer in page : 69

# Study of Relationship Between Non HDL Cholesterol and Severity of Stroke

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Chettinad Health City Medical Journal 2019; 8(2): 62

## Introduction

Dyslipidemia is established as a risk factor for cerebrovascular accidents in various studies. Patients with elevated total cholesterol, LDL cholesterol and decreased HDL cholesterol are at a higher risk of developing stroke. Non HDL cholesterol is total cholesterol minus HDL cholesterol. In a recent analysis of data combined from 68 studies it is found that non-HDL-C was the best predictor among all cholesterol measures, both for coronary artery disease events and for strokes.

## Aim of the Study

To assess the severity of stroke in patients with increased non HDL cholesterol.

## Materials and Methods

It is a cross sectional study of 100 stroke patients, selected based on CT/MRI findings. National Institute Health Stroke Scale (NIHSS) is used to quantify the severity caused by stroke (Mild- 0-7, Moderate- 8-13, Severe- 14-21, Very severe- 22-42). Serum non HDL cholesterol levels were calculated in these patients.

## Results

The mean age of study population is  $59.32 \pm 15.235$  years. Older age, male gender, hemorrhagic stroke, overall co-morbidities, existence of both diabetes and hypertension and elevated non HDL cholesterol was found to be better predictors of severe stroke. The statistically significant predictors of severe stroke included hemorrhagic stroke ( $p=0.041$ ), overall co-morbidities ( $p=0.000$ ), existence of both diabetes and hypertension ( $p=0.000$ ), elevated non HDL cholesterol ( $p=0.001$ ).

## Conclusion

Elevated non HDL cholesterol was established as predictor of severe stroke.

## Key words

Non HDL Cholesterol, Stroke, Hemorrhagic stroke.

### Image Challenge - 07



Clue : Elderly female from west bengal with recurrent abdominal pain and skin pigmentation

- Answer in page : 70

# A Comparative Study of Acute Phase Reactants as Prognostic Marker in Sepsis

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Chettinad Health City Medical Journal 2019; 8(2): 63

## Introduction

Sepsis and septic shock is a common life threatening condition seen in the emergency department. Early identification of sepsis and goal directed therapy is a must for a better outcome in sepsis.

## Aim of the Study

1. To compare the predictive value of acute phase reactants namely -serum ferritin, procalcitonin and CRP level in the prognosis of sepsis.
2. To compare the superiority of ferritin over procalcitonin in predicting the prognosis of sepsis.

## Materials and Methods

This was a cross sectional study which included 86 patients admitted in the ICU of a tertiary care center with sepsis. Informed consent was taken from all subjects and from patient's relatives if patient was unable to give consent. Serum ferritin, procalcitonin and CRP were done immediately after admission and processed within 30 minutes of collection using an auto analyser.

## Results

1. Serum CRP >50 mg/dl and procalcitonin levels >16.1 mcg/dl was correlating significantly with mortality in sepsis.
2. A serum ferritin level >396ng/ml also correlated well with the mortality in sepsis.
3. The sensitivity of these acute phase reactants in predicting mortality in sepsis were high namely - Serum ferritin-75.6%, CRP - 73.2% and Serum procalcitonin- 70.7%.
4. The specificity of predicting mortality in sepsis was highest with procalcitonin & it was low for CRP and ferritin

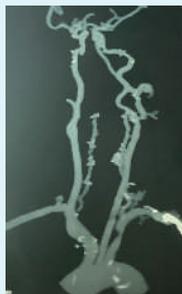
## Conclusion

All three acute phase reactants are similar in predicting the prognosis of subjects in sepsis. Serum Ferritin is not superior to Procalcitonin or CRP in predicting the mortality of patients with sepsis

## Key words

Procalcitonin, CRP, Serum ferritin.

## Image Challenge - 08



Clue : Elderly male presenting with giddiness and left arm claudication

- Answer in page : 71

## A Study of Correlation Between Admission Serum Uric Acid Levels and Short Term (14 Days) Clinical Outcomes in Acute Ischemic Stroke Patients in a Tertiary Care Centre.

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Chettinad Health City Medical Journal 2019; 8(2): 64

### Introduction

There are several studies which project the cerebro-protective effect of uric acid in acute ischemic stroke patients by its antioxidant effect. This study analyses the severity of stroke and short term clinical outcome with reference to serum uric acid levels.

### Materials and Methods

We studied 45 acute ischemic stroke patients who were admitted within 48 hours of onset. The clinical severity of stroke was assessed using NIHSS scale and serum uric acid levels were measured at the time of admission. Then 14 day clinical outcome was reassessed with NIHSS scale and compared. Results were statistically analysed.

### Results

Among 45 patients studied, 29 were male, 16 were female and the mean serum uric acid was 5.89. Mean uric acid levels in males and females were 6.3 and 5.12 respectively. By using NIHSS scale, severity of stroke at the time of admission is less and 14 days outcome of these patients is also better when the uric acid level is higher.

### Conclusion

Our study supported the hypothesis that acute ischemic stroke patients with elevated serum uric acid at the time of admission had reduced severity and favourable short term clinical outcome.

### Key words

Acute ischemic stroke, Uric acid.

### Image Challenge - 01



Answer : CP ange tumour

## A Quality Improvement Initiative on Delayed Cord Clamping

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Chettinad Health City Medical Journal 2019; 8(2): 65

### Introduction

Delayed cord clamping at birth has proven benefit in neonates. The objective of the study was to perform a quality improvement initiative and evaluate adherence to a delayed cord clamping protocol for babies who did not require resuscitation after the introduction of protocol.

### Materials and Methods

To implement and sustain the practice of delayed cord clamping:“WHO point of care quality improvement initiative”model was adapted for this. This study was conducted at Chettinad Hospital& Research Institute, a tertiary care facility with level 3 Neonatal Intensive Care Unit (NICU). All neonates delivered at Chettinad hospital who did not require resuscitation during period of September 2018 to February 2019 were included in the study.

A fish bone analysis was done to assess challenges associated with delayed cord clamping in newborns. The initial 2 months of the study (Baseline phase) was done to assess the practice of delayed cord clamping in newborns. The next 2 months was the implementation phase where multiple plan-do-study-act cycles were done involving obstetricians, neonatologists and staff nurses. Last 2months of the study was to evaluate the sustainment of delayed cord clamping.

### Results

The compliance rate for delayed cord clamping increased to 96%. This had increased from 0% of babies observed before the introduction of quality improvement initiative.

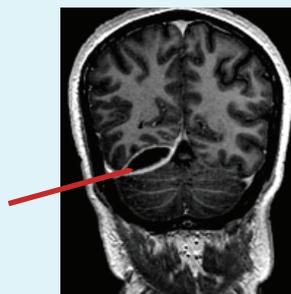
### Conclusion

Sustainment to the practice of delayed cord clamping in newborns was achieved with the help of this initiative.

### Key words

Delayed cord clamping, Neonates, Quality improvement initiative.

### Image Challenge - 02



Answer : Subdural empyema

## To Study the Platelet Indices as Predictive Factors for Microvascular Complications in Type 2 Diabetic Patients in a Tertiary Care Hospital

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Chettinad Health City Medical Journal 2019; 8(2): 66

### Introduction

Platelet indices like total platelet count, mean platelet volume, plateletcrit, platelet distribution width are emerging as good predictors in assessing diabetic patients who are prone for microvascular complications. There are many studies which emphasize the role of platelet indices as a predictor for microvascular complications of diabetes like retinopathy, neuropathy and nephropathy. This study is a comparative study among diabetic population, with and without microvascular complications and analysis of platelet indices in these 2 subgroups, regarding the correlation between abnormal platelet indices and microvascular complications.

### Materials and Methods

Total number of patients studied were divided into 2 groups according to the presence or absence of microvascular complications. Thorough history, clinical examination, investigation necessary for the diagnosis of microvascular complications were done. Platelet indices were done in all patients and results were analyzed.

### Results

Platelet indices were significantly higher in diabetic individuals with microvascular complications when compared with those without microvascular complications.

### Conclusion

Changes in platelet indices were found to be statistically associated with diabetic microvascular complications. Hence these parameters can be used to monitor and predict the risk of microvascular complications.

### Key words

Platelet indices, Microvascular complications, Diabetes mellitus .

### Image Challenge - 03



Answer : Splenic infarct

## Distribution of Infections in Critically Ill Patients in ICU in a Tertiary Care Center

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Chettinad Health City Medical Journal 2019; 8(2): 67

### Introduction

Infectious diseases continue to pose a major public health challenge for the low- and middle-income countries across the world from time immemorial. With increasing awareness and facilities, there has been use of multiple antibiotics which in turn increase the incidence of multidrug resistant organisms.

### Materials and Methods

A clinical, prospective observational study at MGMCRI hospital Intensive care unit. A total of 153 patients admitted in ICU with infections were studied. Demographic, physiological, bacteriological, and therapeutic data were collected on the day of the admission and regularly at prefixed intervals depending upon the patient until hospital discharge.

### Results

A microbiological diagnosis was established less frequently in elderly patients aged 65 and above as compared to those younger than 65. Gram negative organisms were the most common isolates.

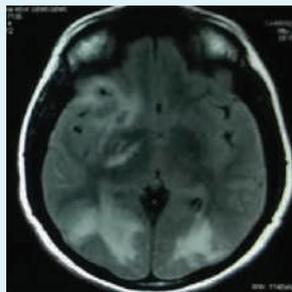
### Conclusion

In our study we found that gram negative infections are more common than gram positive organisms in contrast to the western world and hospitals need to develop hospital specific protocols to fight infections..

### Key words

Distribution of infection, ICU, Gram negative infections.

### Image Challenge - 04



Answer : Multiple ring enhancing lesions - neurocysticercosis

## A Study to Determine the Prognostic Significance of Serum Uric Acid Levels in Acute Ischemic Stroke

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Chettinad Health City Medical Journal 2019; 8(2): 68

### Introduction

Stroke is one of the most common and leading causes of morbidity and mortality in the world. Various studies have shown correlation between the levels of uric acid and acute cerebrovascular disease, although the role of uric acid in pathogenesis of stroke is still controversial.

### Aims and objectives

To determine the prognostic significance of serum uric acid in acute ischemic stroke

### Materials and Methods

This is a cross-sectional study conducted at a tertiary care hospital, Chennai over a duration of 1 year. 50 patients were enrolled. After obtaining a detailed history, a complete general, physical and systemic examination, patients were subjected to relevant investigations with informed consent. Serum uric acid levels were drawn at the time of admission.

### Results

Mean serum uric acid in patients with poor outcome (6.27 mg/dl) was higher than patients with a good outcome (5.31 mg/dL). There is a significant association (P value < 0.001) between increased serum uric acid levels and poor outcome in acute ischemic stroke.

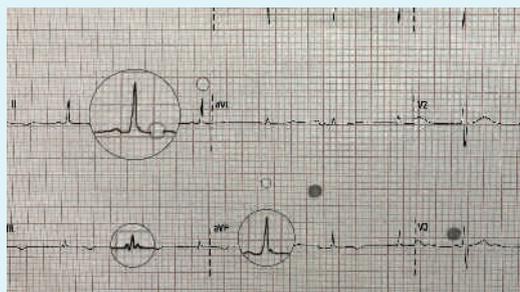
### Conclusion

Stroke patients with elevated serum uric acid levels had a poor outcome. Uric acid is the most abundant antioxidant in humans and uric acid concentrations increase during acute oxidative stress and ischemia, especially in acute brain injury. In acute ischemic stroke, uric acid can be considered as a biochemical marker of oxidative stress..

### Key words

Stroke, Uric acid, Prognosis.

### Image Challenge - 05



Answer : Epsilon wave

## Thyroid Function Test and its Relation to Chronic Kidney Disease

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Chettinad Health City Medical Journal 2019; 8(2): 69

### Introduction

Patients with chronic kidney diseases have many symptoms and signs suggestive of thyroid dysfunction. It is very difficult to exclude the diagnosis of hypothyroidism on clinical grounds. So a study was conducted in CKD patients to study the prevalence and types of thyroid dysfunction and the correlation between thyroid dysfunction and severity of renal insufficiency if any.

### Materials and Methods

The study was designed to study one hundred and ten patients who had been diagnosed with chronic kidney disease. The subjects were those who attended the outpatient and inpatient department in Mahatma Gandhi Medical College and Research Institute, Pondicherry. A detailed history and clinical examination were done. Investigations including urea, creatinine, serum T<sub>3</sub>, T<sub>4</sub>, TSH were done.

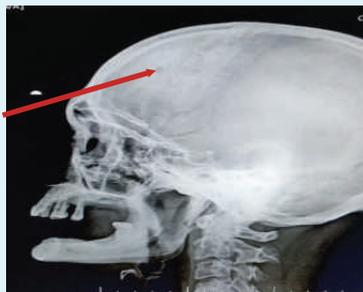
### Results

Thyroid dysfunctions were present in chronic kidney disease patients in this study which was more in stages four and five. Thyroid dysfunction occurs both clinically and biochemically in CKD. Subclinical hypothyroidism and non-thyroid illness were the commonest. Number of patients with non-thyroid illness progressively increases with severity of renal failure.

### Key words

Chronic kidney disease, Sub clinical hypothyroidism.

### Image Challenge - 06



Answer : Punched out lesion

# A Study of Serum Magnesium Levels in Diabetic Patients admitted to Medical ICU

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Chettinad Health City Medical Journal 2019; 8(2): 70

## Introduction

Magnesium is fourth most common cation in the body and second most common intracellular cation after potassium, yet its deficiency in critically ill patients is frequently overlooked. Diabetes mellitus is known to cause loss of magnesium in the urine, associated with glycosuria, which further lowers magnesium in the plasma of diabetic patients, aggravating the risk of development of its complications. So the present study is designed to reveal the relation between low magnesium levels during critical illness and their predictability in the outcome of intensive care therapy.

## Aims and Objectives

- 1) To study serum magnesium levels in critically ill patients admitted in medical intensive care unit.
- 2) To correlate serum hypomagnesemia in critically ill, diabetic and non-diabetic patients admitted in a medical intensive care unit and to compare their mortality.

## Materials and Methods

A cross sectional study was done in 60 patients admitted in medical intensive care unit in a tertiary care hospital. Diabetic patients and non-diabetic patients, with or without previous history of any hypertension and or vascular disease and or renal disease and or cardiovascular disease, were studied.

## Results

60 patients admitted in medical intensive care unit were enrolled in this study of which 37 were diabetic and 23 non diabetic. The mean age of study population is 59.85. Patients were monitored throughout the ICU stay and were divided into survivors and non survivors. Mortality rates among diabetic patients who had hypomagnesemia was significantly more when compared with diabetic patients without hypomagnesemia (p value < 0.05).

## Conclusion

Hypomagnesemia is a common electrolyte imbalance in patients admitted in medical intensive care unit. It was frequently associated with diabetes mellitus and incidence of hypomagnesemia correlated with increased duration of diabetes. Mortality was significantly higher in patients with diabetes mellitus and hypomagnesemia than without diabetes mellitus without hypomagnesemia.

## Key words

Hypomagnesemia, Diabetes mellitus, Intensive care unit.

### Image Challenge - 07



Answer : Rain drop pigmentation of Arsenic poisoning

## Does Hypomagnesemia Predict Mechanical Ventilator Requirement and Outcome in Intensive Care Unit?

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Chettinad Health City Medical Journal 2019; 8(2): 71

### Introduction

Hypomagnesemia can result in well known complications like ventricular arrhythmia, convulsions, neuro-muscular weakness, inability to wean off the ventilator and severe metabolic abnormalities. As magnesium being an unrecognized entity in critically ill patients, a study was done to observe hypomagnesemia and its association with hypokalemia, hypocalcaemia, ventilator requirement and outcome in intensive care unit (ICU)

### Materials and Methods

Prospective study done in medicine ICU including all patients admitted to ICU with duration of stay more than 2 days and magnesium levels <1.8 mg/dl during the first 24 hours.

### Results

The incidence of hypomagnesemia in critically ill patients in this study was 15.83%(169 patients).Magnesium in association with serum potassium and calcium showed positive correlation but the observation was not statistically significant.Magnesium in association with ICU stay showed negative correlation but the observation was not statistically significant(mean stay-4.85 days p=0.093).Magnesium in association with Ventilator requirements showed that there was statistically significant requirement of mechanical ventilation in patients with hypomagnesemia(62 patients mean=1.474 p=0.001).

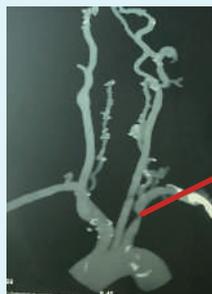
### Conclusion

As hypomagnesemia has a significant association with adverse outcomes, we suggest that measurement of magnesium to be done in all critically ill patients in ICU.

### Key words

Hypomagnesemia, Mechanical ventilator, ICU.

### Image Challenge - 08



Answer : Subclavian artery stenosis

# Correlation of Carotid Artery Stenosis with Diabetes Mellitus & Hypertension in Acute Ischemic Stroke

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Chettinad Health City Medical Journal 2019; 8(2): 72

## Introduction

Stroke remains the second leading cause of death world wide, after ischaemic heart disease. 85% of stroke cases are due to infarction and 15% are due to haemorrhage. Carotid atherosclerosis remains an important cause of ischaemic stroke. Carotid atherosclerosis occurs in patients with atherosclerotic risk factors like diabetes mellitus, hypertension. It leads to plaque formation which increase in size and causes stenosis.

## Materials and Methods

This is a hospital based cross sectional single centre study in 100 patients with acute ischemic stroke

## Results

It has been noted that the prevalence of carotid stenosis in this study is 58% where in of the 75 patients with the carotid doppler, 44 were observed to have stenosis while 31 didn't. There was a correlation between diabetes mellitus and carotid stenosis. More diabetes mellitus patients had carotid stenosis than non diabetic which was statistically significant ( P value < 0.001). Prevalence of carotid stenosis was more in hypertensives than in nonhypertensives and it was statistically significant ( P < 0.001)

## Conclusion

The prevalence of carotid stenosis increases with diabetes mellitus and hypertension .A simple, non invasive screening procedure like doppler sonography of the carotid arteries in high risk individuals could therefore have profound diagnostic and therapeutic implications in predicting and preventing a potentially fatal and devastating stroke.

## Key words

Stroke , Hypertension, Diabetes.

## Interesting Image



\*Do you know the importance of this place?

See Page : 93

## Abstracts - Posters

### An Unusual Case Of Dermatomyositis Associated With Multiple Angiolipomas

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Chettinad Health City Medical Journal 2019; 8(2): 73

#### Abstract

Dermatomyositis is a chronic inflammatory immune mediated disorder of skin and muscles. Patients with classic dermatomyositis typically present with symmetric, proximal muscle weakness, and skin lesions that demonstrate interface dermatitis on histopathology. We report a 39 year old female who presented with painful proximal myopathy with multiple joint pain. She had hyperpigmented rashes over forehead, nasal bridge and anterior wall of chest. On examination there were multiple painful small nodules over joints with restriction of movements. Excision biopsy showed features consistent with angiolipoma. Musle biopsy report favoured diagnosis of dermatomyositis and she was started on injection methotrexate.

#### Key words

Dermatomyositis, Angiolipomas, Methotrexate

### Priapism Following Scorpion Sting: A Cardiac Premonitory Sign

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Chettinad Health City Medical Journal 2019; 8(2): 73

#### Abstract

A 3 year old boy presented with a history of scorpion bite. He presented with severe pain at the site of sting and vomiting. On arrival, the child had no respiratory distress but he was irritable, diaphoretic and had priapism. His heart rate was 138 beats per minute and blood pressure was 126/84 mmHg. He was managed with oxygen via mask and Jackson-Rees circuit, IV normal saline 5ml/kg and tablet Prazosin 0.5 mg. He was monitored in the MICU for signs of myocarditis. Eventually he became hypotensive and developed pulmonary edema due to myocarditis. He was managed with non invasive positive pressure ventilation and dobutamine. He was gradually weaned of inotropes. Fatality rate is highest in the first 24 hours after scorpion sting due to respiratory or cardiovascular failure following alpha receptor stimulation by the toxin. Adequate fluid replacement and inotropic support improves hypotension. Anti venom therapy does not prevent the cardiovascular manifestation. Prazosin blocks post synaptic alpha 1 receptors. Presence of priapism (Grade 3 envenomation) correlates positively with occurrence of myocarditis. Hence children with scorpion sting should be observed for myocarditis especially in the presence of priapism.

#### Key words

Scorpion sting, Priapism, Myocarditis.

## Post Varicella Cerebellitis – A Case Report

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Chettinad Health City Medical Journal 2019; 8(2): 74

### Abstract

Varicella is an acute, exanthematous, and highly infectious disease affecting virtually every child in the absence of vaccination programs. Varicella has mostly an uncomplicated course in early childhood. Nevertheless, it may result in severe complications. Among neurological complications, acute cerebellitis was the most frequent manifestation. 15 Year old girl, with history of varicella zoster infection 2 months ago, presented with complaints of swaying while walking since 2 weeks. General examination revealed skin lesions in the chest and back regions. On systemic examination, she was found to have positive cerebellar signs bilaterally and no motor weakness or sensory disturbances. All routine blood investigations were found to be normal. MRI brain showed features of acute bilateral cerebellitis, mildly dilated bilateral lateral ventricles and 3rd ventricle. Patient was started on intravenous corticosteroids. After 2 weeks of immunosuppressive therapy, patient showed improvement of her involuntary movements and ataxia. Repeat MRI brain revealed complete resolution of lesion in the right cerebellar hemisphere, very minimal residual hyperintensity in the posterior aspect of left cerebellar hemisphere and no evidence of hydrocephalus.

### Key words

Varicella zoster, Cerebellitis, Ataxia, Immunosuppressive therapy

## A Case Of Down's Arthropathy

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Chettinad Health City Medical Journal 2019; 8(2): 74

### Abstract

A 35 yr old male, who is known case of Down's syndrome with complex congenital heart disease and hypothyroidism presented with pain and swelling of right knee and ankle joints. Musculoskeletal examination revealed features of right knee arthritis and hyperflexibility of left hip joint. Investigations revealed polycythemia and elevated CRP - 11.48. Synovial fluid analysis was done and reports did not show evidence of gouty or tubercular arthritis. Reports showed elevated LDH, ADA and total count. Thus we arrived at a final diagnosis of Down's arthropathy. Literature states that Down's arthropathy is rarely recognized and under diagnosed but is more common than juvenile idiopathic arthritis. Hence patients with Down's syndrome may have various causes of arthritis but a diagnosis of Down's arthropathy is always a possibility.

### Key words

Downs arthropathy, Juvenile idiopathic arthritis.

## A Case Of Double Fever

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Chettinad Health City Medical Journal 2019; 8(2): 75

### Abstract

Malaria and dengue are commonest vector borne diseases in India. Due to similar clinical presentations of malaria and dengue, these co-infections may give rise to an incorrect diagnosis or may be difficult to diagnose. Areas where both vectors co-exist, double infection cannot be ruled out. A 40 year old male with no comorbidities came with generalised tiredness since 1 week, high grade fever with chills and rigors since 4 days and abdominal pain since 4 days. On examination he was febrile and had tachycardia, tachypnoea, and hypotension. Icterus was present. Bilateral rhonchi and hepatomegaly were observed. Investigations were done and he was diagnosed as a case of malaria and dengue. Patient was started on IV fluids, antimalarials, antipyretics and other symptomatic measures. Patient gradually improved during the course of hospital stay.

### Key words

Malaria, Dengue, Double fever

## Dabigatran Induced Adrenal Hemorrhage

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Chettinad Health City Medical Journal 2019; 8(2): 75

### Abstract

Dabigatran is used in the treatment and prophylaxis of deep venous thrombosis, pulmonary embolism and in non valvular atrial fibrillation. It causes bleeding in 11-19%. We report a case of adrenal hemorrhage due to dabigatran. A 49 year old male presented with epigastric pain for one day. He had prior history of hereditary spherocytosis and was on T.Dabigatran 150mg twice daily for recent deep venous thrombosis. On examination vitals are stable, mild pallor, icterus were present. In the ward, he suddenly developed giddiness, profuse sweating and was found to have tachycardia of 110/min and hypotension of 80/50 mmHg. There is sudden drop in hemoglobin and platelets. Serum cortisol was <0.4 µg/dl. CT scan of abdomen revealed bulky bilateral adrenal gland with hemorrhage. Initially patient was managed with bolus IV fluids; one packed red blood cell transfusion was done and was started on injection hydrocortisone. He was discharged with oral steroids. Since continuous anticoagulation was required for deep venous thrombosis, after discussing the consequences of dabigatran, it was restarted after 4 weeks.

### Key words

Dabigatran, Bilateral Adrenal Haemorrhage, Deep vein thrombosis

## Hemoglobinopathies Diagnosed In Uncommon Geographic Region.

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Chettinad Health City Medical Journal 2019; 8(2): 76

### Abstract

Hemoglobinopathies are not so common in the northern part of Tamil Nadu. However, within a short span of two months we have diagnosed three patients with hemoglobinopathies. Two patients were from the migrant population of Kelambakkam. One patient was native of Tamil Nadu. For all the three patients EDTA sample for CBC was collected. In the patient native to Tamil Nadu, sickle cells were seen in the peripheral smear together with target cells and Howell Jolly bodies. One patient showed mild anemia of 9.5gm/dL and the other patient showed normal hemoglobin of 13.2gm/dL. In both these patients there was a relative erythrocytosis with a low MCV and MCH. The high performance liquid chromatography (HPLC) for hemoglobin variant analysis showed homozygous sickle cell disease in the first patient. The second patient showed a band of 87.5% of unknown variant ?HbD Punjab and HbA2 of 4.4% suggestive of HbD Punjab/ Beta thalassemia trait. The third patient showed HbA2 of 6.2% and was diagnosed as heterozygous beta thalassemia trait.

### Key words

Hemoglobinopathies, HbD Punjab, Sickle cell

## Topiramate Induced Acute Angle Closure Glaucoma

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Chettinad Health City Medical Journal 2019; 8(2): 76

### Abstract

Topiramate is an anticonvulsant used in the treatment of epilepsy, vertigo and migraine prophylaxis. Acute angle closure glaucoma is a known side effect of topiramate. We present a 42 year old male who was started on topiramate 25 mg/day for vertigo. He presented with severe headache since 1 day after nine days of starting topiramate. On examination, vision was 6/6. Both eyes showed clear corneas, shallow anterior chambers, clear lens and reactive pupils. Intraocular Pressure was 56 mmHg in right and 52mmHg in left eye. Gonioscopy showed closed angles. Considering the bilateral involvement and history of taking topiramate, diagnosis of topiramate induced AACG was made. Topiramate was stopped and patient was started on I.V mannitol, timolol, brimonidine, prednisolone eye drops, diamox. Patient started improving from second day and IOP became normal in 4 days with normal angles on gonioscopy. A high index of suspicion and prompt management in topiramate induced bilateral AACG helps in quick and complete visual recovery.

### Key words

Topiramate , Acute angle closure glaucoma , Anticonvulsants

## The Silence Of The Lungs

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[Chettinad Health City Medical Journal 2019; 8\(2\): 77](#)

### Abstract

Primary spontaneous pneumothorax (PSP) occurs in otherwise healthy individuals. It is more common in tall statured, males, smokers and in presence of blebs. Recurrence rate of PSP is 29% at 1 year on same side with contralateral being 16%. A 19 year old male smoker with marfanoid features presented with left sided chest pain and breathlessness. Examination revealed decreased air entry in the left hemithorax. Chest xray showed left sided pneumothorax. CT chest showed pneumothorax on the left side and bilateral sub pleural apical blebs. Intercostal drainage was placed to relieve dyspnea. Patient quit smoking. 1 month later, the patient presented with similar complaints. In view of left hydropneumothorax, ICD drainage and pleurodesis were done. Patient was symptom free for 6 months and presented with contralateral hydropneumothorax. ICD drainage was done but he refused pleurodesis. Patient is symptom free with no recurrence in 3 years follow up. The recurrence is more in women (71%); smoking cessation reduces risk of recurrence by fourfold. This case is being presented to highlight the recurrence of pneumothorax within 6 months.

### Key words

Primary spontaneous pneumothorax, Smokers, Blebs.

## A Rare Case Of Posterior Reversible Encephalopathy Syndrome

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[Chettinad Health City Medical Journal 2019; 8\(2\): 77](#)

### Abstract

Posterior reversible encephalopathy syndrome (PRES) is a syndrome characterised by headache, confusion, seizures and visual loss. It can present as status epilepticus also. Most common causes are malignant hypertension, eclampsia, renal failure and drugs (immunosuppressants like cyclosporine and tacrolimus). Our case is a 36yr old male patient with no known comorbid illness, came with complaints of giddiness, blurring of vision and seizures. At the time of presentation, his blood pressure was 220/140mmHg. Fundus evaluation showed bilateral established papilledema. MRI brain showed features of posterior reversible encephalopathy syndrome with cervical cord involvement. Investigation showed deranged renal parameters. Ultrasound abdomen showed right contracted kidney. MR angiogram revealed right renal artery stenosis and renal artery angioplasty was done. Posterior reversible encephalopathy syndrome with cervical cord involvement is a rare entity. Malignant hypertension secondary to renal artery stenosis is the commonest cause of posterior reversible encephalopathy syndrome (PRES) in males and eclampsia is the leading cause in females.

### Key words

Posterior reversible encephalopathy syndrome, Malignant hypertension, Renal artery stenosis.

## An Interesting Presentation Of Subclavian Steal Syndrome

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Chettinad Health City Medical Journal 2019; 8(2): 78

### Abstract

Subclavian steal syndrome is a constellation of signs and symptoms that arise from retrograde blood flow in the vertebral artery or the internal thoracic artery due to a proximal stenosis or occlusion of subclavian artery. The increased metabolic demand of left or right arm musculature during exercise is met by retrograde blood flow down the vertebral artery and results in symptoms of brain stem ischemia. Patients usually presents with syncope, unequal pulses, anisophygma between 2 upper limbs. We report a case of 55 year old male who presented with the symptoms of posterior circulation stroke and eventually diagnosed as a case of left subclavian steal syndrome.

### Key words

Subclavian steal, Syncope, Brainstem ischemia, Posterior circulation stroke.

## An Interesting Case Of Sero-Negative Systemic Sclerosis

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Chettinad Health City Medical Journal 2019; 8(2): 78

### Abstract

Systemic sclerosis is a chronic progressive multisystem disease involving skin, lungs, heart, gastrointestinal tract associated with autoimmune antibodies in serum (90%). We report an interesting case of 48 year old female who is a known case of type 2 diabetes mellitus and coronary artery disease, presented with difficulty in breathing, abdominal distension, vomiting, loose stools, dizziness and easy fatigability. On examination systemic sclerosis features were present. ECG showed sick sinus syndrome. Computed tomography of chest revealed interstitial lung disease. Patient is clinically diagnosed to have systemic sclerosis but ENA profile was negative. Hence diagnosis of sero-negative systemic sclerosis was made.

### Key words

Systemic sclerosis, Interstitial lung disease, Sick sinus syndrome

## A Case Of Hepatobiliary Manifestation Of Inflammatory Bowel Disease—A Case Report

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[Chettinad Health City Medical Journal 2019; 8\(2\): 79](#)

### Abstract

Liver and biliary tract is one of the most common site of extra-intestinal manifestations of inflammatory bowel disease. Primary sclerosing cholangitis is the most common and specific one. Approximately 5% of patients with ulcerative colitis have primary sclerosing cholangitis. This is a case report of a 30 year old male patient presented with complaints of loose stools for last 3 years which gradually increased in frequency from 3-4 times to 6-7 times/day, semi-solid in consistency, yellow in colour, associated with blood and mucus. History of passage of stools during night 3-4 times/day. History of pain abdomen, jaundice and pruritus were present for last 1 year. On examination icterus was present and abdominal examination was normal. Blood investigation showed altered liver function test and ANA positive. Sigmoidoscopy revealed features of ulcerative colitis. MRCP showed early primary sclerosing cholangitis.

### Key words

Ulcerative colitis, Extra-intestinal manifestations, Primary sclerosing cholangitis.

## Catch Me If You Can

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[Chettinad Health City Medical Journal 2019; 8\(2\): 79](#)

### Abstract

Disseminated TB is defined as tuberculous infection involving the blood stream, bone marrow, liver, or 2 or more noncontiguous sites. A 37 year old lady presented with left sided chest pain for 1 year and fever for 1 month duration. There was history of significant weight loss. Chest xray showed bilateral lower zone reticulonodular pattern. Mantoux test was strongly positive (>20mm). Sputum AFB, gene Xpert were negative. Bronchoscopy showed narrowing and hyperemia of left lower lobe bronchus - features suggestive of inflammatory pathology. CECT chest showed multiple lytic lesions in right 9th rib, left 6th rib, sacrum and lumbar vertebra, and 2 retrosternal lesions adjacent to xiphisternum. Multiple necrotic nodes in peripancreatic, paraaortic and retrocaval regions were noted. Multiple scattered nodules were seen in both lungs, hepatic and splenic parenchyma. She was started on ATT based on clinical diagnosis and patient showed clinical and radiological improvement. Disseminated tuberculosis should always be considered in differential diagnosis of patients with suggestive clinical and imaging findings after ruling out malignancy and other respiratory diseases.

### Key words

Disseminated tuberculosis, Multiple lytic lesions, Reticulonodular pattern.

## Characteristic Four!!!

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Chettinad Health City Medical Journal 2019; 8(2): 80

### Abstract

Gerstmann syndrome is a rare neurological disorder that can occur as the result of brain injury or as a developmental disorder. The syndrome is characterized by the loss or absence of four cognitive abilities. It does not run in families. Developmental form is usually accompanied by other cognitive abnormalities also. Adult onset generally presents as a pure form of gerstmann syndrome. A 65 year old male who was a known case of systemic hypertension was brought with history of one episode of involuntary movements of upper limb and lower limb. After this episode he was disoriented and confused for 2 hours. There was no associated headache, fever, vomiting or weakness. On examination, he was found to have finger agnosia, acalculia, agraphia and right left disorientation. MRI Brain revealed a focal subcortical white matter change in the left parietal lobe suggestive of space occupying lesion. He was advised surgery but patient was not willing hence supportive management was continued.

### Key words

Gerstman Syndrome, Finger agnosia, Acalculia, Agraphia, Right left disorientation

## Bullous Impetigo Presenting As Circinate Lesion

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Chettinad Health City Medical Journal 2019; 8(2): 80

### Abstract

A 10 months old female baby reported with oozing lesions over the right side of the chest and left cheek for the past 3 days. There was history of fluid filled lesions 5 days ago which ruptured to form annular lesions. Itching was present. No history of fever or upper respiratory tract symptoms. On examination a single annular plaque with well defined, raised borders with collarette of scaling, oozing and crusting was present over the right side of the chest. Central clearing was present. A round to oval, well defined, oozing, annular plaque with erythematous base was present over the left cheek. Gram stained smear of the discharge revealed the presence of gram positive cocci in clusters, most probably Staphylococcus aureus. Diagnosis of Bullous Impetigo was made. Mupirocin 2% ointment BD, Syp .Cephalexin 5ml BD for 5 days was given. Topical and oral antibiotics are advised for mild cases. In severe cases, hospitalization is advised along with parenteral antibiotics.

### Key words

Staphylococcus, Collarette, Annular, Bullous impetigo.

## Extensive Verruca Vulgaris In A Patient With No Comorbidities

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Chettinad Health City Medical Journal 2019; 8(2): 81

### Abstract

A 48 year old female patient presented with multiple verrucous growths over both hands, forearms, neck, back and face for the past 2 years. There was history of appearance of a single verrucous papule over the right thumb before 2 years which slowly increased in size and became more warty and verrucous, along with appearance of new similar lesions over both hands, forearms, face, neck and back. No known comorbidities and family history was insignificant. Multiple verrucous irregular papules were present over dorsum of both hands, forearms, back of the neck, midline over the back, face. Complete blood count, liver function tests, renal function tests, urine routine, random blood sugar were normal. Histopathological examination showed acanthosis with proliferative hyperkeratotic cells with finger like projections. RF cautery was done and patient was advised follow up after 2 weeks. Since there were no associated comorbidities, the extensive lesions are mostly due to autoinoculation of infected lesions to other areas resulting in widespread lesions elsewhere in the body.

### Key words

Verruca vulgaris, Acanthosis, Human papilloma virus, Hyperkeratosis.

## An Unusual Case Of Asymptomatic Intracranial Abscess

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Chettinad Health City Medical Journal 2019; 8(2): 81

### Abstract

Subdural empyema is a life-threatening complication of paranasal sinusitis, otitis media and mastoiditis. It is more likely to collect over convexities of cerebral hemispheres, in parafalcine region and above tentorium cerebelli. About 95% of subdural empyema involves the frontal lobe, and 5% involves the spinal neuraxis. It develops as a result of either retrograde spread of infection from septic thrombophlebitis of mucosal veins draining the sinuses or from osteomyelitis of skull. It can also develop from direct implantation of bacteria following neurosurgical procedure. We report an interesting case of asymptomatic subdural empyema secondary to chronic suppurative otitis media. A 37 year old male with right chronic suppurative otitis media presented with high grade intermittent fever with chills, rigors and headache, not relieved on taking medications. On examination right ear had mucopurulent discharge and right tympanic membrane had bulge in postero superior quadrant. MRI brain showed subdural empyema in right tentorial leaflet and mastoiditis with erosive changes in tegmen tympani.

### Key words

Chronic suppurative otitis media, Subdural empyema, Asymptomatic intracranial abscess

## A Rare Case Of Polyneuritis Cranialis Due To Diabetes Mellitus

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Chettinad Health City Medical Journal 2019; 8(2): 82

### Abstract

Polyneuritis cranialis is a rare disorder in which multiple cranial nerves palsies without spinal cord involvement is seen. It usually affects VI, III, VII and V cranial nerves. The most common causes are oculo-pharyngeal variant of Guillain-Barre syndrome, lyme disease, herpes zoster, diabetes mellitus, thyrotoxicosis, and idiopathic. We report a case of 55 year old male with uncontrolled type 2 diabetes mellitus for the past 10 years who presented with left sided temporal headache for 2 weeks, numbness over the left half of the face and diplopia for 1 week. On examination patient was found to have unilateral IIIrd, IVth, VIth, Vth, VIIth, and VIIIth cranial nerves palsies. Rest of the examination was unremarkable. MRI Brain showed thickening and enhancement of V, VII, IX cranial nerves. The most common differential diagnosis for the above findings are metastasis, neurofibromatosis type II, lymphoma, multiple sclerosis and basal meningitis. After excluding all the above causes, uncontrolled diabetes mellitus was considered as a cause of polyneuritis cranialis. This case is reported because of rarity of presentation of diabetes mellitus involving only unilateral cranial nerves.

### Key words

Polyneuritis cranialis, Unilateral cranial nerves palsies, Uncontrolled diabetes mellitus

## Could This Be Crow Fukase Syndrome?

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Chettinad Health City Medical Journal 2019; 8(2): 82

### Abstract

Crow Fukase syndrome commonly suggested by the acronym POEMS is seen with progressive sensorimotor polyneuropathy, diabetes mellitus (50%), primary gonadal failure (70%) and plasma cell dyscrasia, with associated findings like hepato-splenomegaly, lymphadenopathy and hyperpigmentation. We report a 45 year old male, a hypertensive who presented with claudication pain in bilateral lower limbs, generalized weakness, unquantified weight loss and anorexia. He was malnourished with bilateral significant axillary lymphadenopathy, bilateral pitting pedal edema with tenderness over both ankle and hepato-splenomegaly. Baseline investigations were normal except for serum creatinine of 1.5 and proteinuria. Doppler of lower limb arteries showed saccular aneurysm in posterior wall of left common femoral artery. CT abdomen with peripheral angiogram showed hepato-splenomegaly with multiple sclerotic lesions and multiple hyper enhancing lymph nodes. NCS showed sensory neuropathy of lower limbs, demyelinating sensorimotor neuropathy of bilateral ulnar nerves, bilateral median nerve entrapment, following which possibility of POEMS was considered which was confirmed with serum immune-fixation and bone marrow biopsy. The close differentials for this patient were Castleman disease and osteosclerotic variant of multiple myeloma. However, POEMS was confirmed and the patient was started on MDex regimen. Patient is doing well after three cycles of chemotherapy.

### Key words

Crow Fukase syndrome, POEMS, Primary gonadal failure.

## A Rare Case Of Vitamin B 12 Deficiency Masquerading Addison's

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Chettinad Health City Medical Journal 2019; 8(2): 83

### Abstract

A 37 Year old female presented with hyperpigmentation of tongue, bilateral hands and foot, generalised fatigue, weight loss with history of abdominal tuberculosis and she was on category I ATT for 4 months. She was a known case of hypothyroidism and sero-negative polyarthritis. On examination she was pale, hyperpigmentation was noted on tongue, both hands and toes. She was hypotensive. Systemic examination was normal. Initially we suspected adrenal insufficiency, but her serum cortisol was 14mcg/dl. In view of pancytopenia and raised MCV (112.3) possibility of vitamin B12 deficiency was considered and levels were found to be very low (47pg/ml) and peripheral smear showed macrocytic anemia with hypersegmented neutrophils and thrombocytopenia. Hyperpigmentation resolved with vitamin B12 supplementation.

### Key words

Hyperpigmentation, Adrenal insufficiency, Vitamin B12 deficiency.

## Malignant Mycobacterium Mischap

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Chettinad Health City Medical Journal 2019; 8(2): 83

### Abstract

Pulmonary tuberculosis (TB) and bronchogenic carcinoma often may have overlapping clinical features like weight loss, anorexia, cachexia, chronic cough and chest pain. Around 2-4% of TB cases are coexisting with malignancy. Current case presented highlights co-existence of bronchogenic carcinoma and pulmonary TB. A 70 year old male presented with cough, fever, breathlessness and right sided chest pain for 1-month. Chest x-ray showed homogenous opacity in right lower zone, blunting of costophrenic angle and non-homogenous cavitary opacity in left upper zone. Sputum AFB was negative, but gene xpert was positive for mycobacterium tuberculosis (rifampicin sensitive). Pleural fluid was exudative and cytology showed malignant cells. CECT thorax revealed right middle lobe mass with mediastinal, bilateral hilar lymph nodes, right pleural effusion and consolidatory collapse of right lower lobe. Thoracoscopy showed scattered nodules in visceral, costal and diaphragmatic pleura with parietal pleural adhesion. Biopsy revealed adenocarcinoma. Presence of risk factors like smoking, immunosuppression and contact history of TB should alert clinician for considering diagnosis of TB and lung cancer coexistence especially in high burden TB country like India.

### Key words

Pulmonary tuberculosis, Bronchogenic carcinoma, Smoking

## A Case of Drug Induced Refractory Hypokalemia with Acidosis

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Chettinad Health City Medical Journal 2019; 8(2): 84

### Abstract

Cisplatin and its derivatives are traditionally the first-line chemotherapy drugs in most of the cancers. Platinum chemotherapy, particularly cisplatin, is commonly associated with electrolyte imbalances, including hypomagnesaemia, hypokalemia, hypophosphatemia, hypocalcaemia and hyponatremia. We report an unusual case of 60 year old male post subtotal gastrectomy patient for carcinoma stomach two months ago, who presented with abdominal pain and loose stools for 3 days, vomiting for one day. On examination pulse rate was 65 per minute, blood pressure was 170/100mmHg. Arterial blood glass showed lactic acidosis. Electrocardiogram, cardiac enzymes and ECHO were normal. Patient was started on electrolyte correction. Despite intravenous electrolyte correction the patient remained hypokalemic. During the hospital stay patient developed hypotension and started on inotropic support. Patient went in for cardiac arrest; resuscitation attempted, patient's condition initially improved and then worsened, and later expired.

### Key words

Cisplatin, Refractory hypokalemia, Carcinoma Stomach.

## Open Rings Of Demyelination: A Rare Case Of Tumefactive Multiple Sclerosis

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Chettinad Health City Medical Journal 2019; 8(2): 84

### Abstract

Multiple sclerosis is an autoimmune disorder characterised pathologically by chronic inflammation, demyelination, neuronal loss and gliosis and clinically as a relapsing remitting or progressive neurological deficit. The neurological deficit in multiple sclerosis is predominantly sensory and is often associated with optic neuritis. Tumefactive multiple sclerosis, is a rare variant of multiple sclerosis, occurring in 1/1000 case of multiple sclerosis. It is characterised by MRI findings resembling space occupying lesions, consisting of large plaques of more than 2cm size with perilesional oedema and mass effect. Clinical presentation is atypical of multiple sclerosis, and is more reflective of space occupying lesions. But rarely these patients can also present with stroke (1-2%). We report a case of a 30 year old blind female who presented with features of stroke; acute onset right sided hemiparesis, right hemi-sensory loss and left sided lower motor neuron type facial palsy following a right focal seizure. MRI Brain with contrast showed multiple open ring enhancing lesions involving bilateral cerebral hemispheres, left pons and left middle cerebellar peduncle. But unlike a vascular stroke, neurological deficits improved with pulse methyl prednisolone therapy. Tumefactive multiple sclerosis can thus mimic clinical and radiological features of a stroke, neoplasm or abscess and therefore can be diagnostically challenging for clinicians.

### Key words

Tumefactive lesions, Open Ring Enhancing Lesions, Multiple sclerosis

## A Rare Case of Immune Reconstitution Inflammatory Syndrome in Immunocompetent Individual

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Chettinad Health City Medical Journal 2019; 8(2): 85

### Abstract

Immune reconstitution inflammatory syndrome represents a clinical phenomenon of immune mediated inflammation against various antigens like mycobacteria, herpes, drugs and unknown autoantigens during recovery from immunosuppressed conditions. We report a 29 year old female who presented for evaluation of pyrexia of unknown origin. She was started on anti-tuberculosis treatment in view of a positive sputum gene xpert for mycobacterium tuberculosis. Her HIV status was negative. Patient responded transiently but again deteriorated clinically. PET scan showed mediastinal lymphadenopathy with hepatosplenomegaly. After ruling out other causes of fever, immune reconstitution inflammatory syndrome was diagnosed as she improved only with oral steroids. Immune reconstitution in pulmonary tuberculosis in non-HIV settings has been reported in 2.4% of patients.

### Key words

Immune reconstitution inflammatory syndrome, Pyrexia of unknown origin, Tuberculosis, GeneXpert, Steroids

## A Case Of Acute Intermittent Porphyrria - An Obstetric Challenge

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Chettinad Health City Medical Journal 2019; 8(2): 85

### Abstract

Acute intermittent porphyria is a rare autosomal dominant disease (1-2/200000) caused by mutation in the gene coding for the porphobilinogen deaminase enzymes in heme biosynthesis. The disease manifests as acute attacks of neuropsychiatric dysfunction and neurovisceral manifestations presenting as acute abdomen. We report a 21 year old female primigravida at 37 weeks 4 days of gestational age who was a known case of acute intermittent porphyria with anemia (Hb-7.1gms/dl) admitted for safe confinement. 3 years back she had complained of abdominal and lower limb pain for which she was admitted and evaluated during which she had an episode of seizure. MRI brain and CSF analysis were normal. Her ALA was 50.9 and porphobilinogen was 54.9mg/day. Since her haemoglobin was low, one unit of packed red blood cell transfusion was given. In view of cephalopelvic disproportion, patient was taken up for caesarean section and delivered an alive healthy male baby of 2.66Kgs.

### Key words

Porphyria, Acute abdomen, Porphobilinogen.

## Antiphospholipid Antibody Syndrome

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Chettinad Health City Medical Journal 2019; 8(2): 86

### Abstract

Antiphospholipid antibody syndrome is a thrombotic disorder, defined by the presence of one or more clinical features of thrombosis and presence of antiphospholipid antibodies such as anti cardiolipin, anti beta2 GP1 and or lupus anticoagulant. This syndrome is also known as Hughe's syndrome. A 26 year old female, G3P1L1A2 was admitted with complaints of loose stools and pain abdomen for 4 days. Systemic examination was normal. There were no manifestations to suggest bleeding diathesis. Ultrasound abdomen showed portal vein and SMV thrombosis, bulky uterus with retained products of conception. Gynaecologist suggested elective termination of the current pregnancy. CECT abdomen was done which showed thrombosis of the superior mesenteric vein, splenic vein and portal vein. In view of recurrent abortions and thrombotic manifestations, workup for APLA was sent. Anticardiolipin antibodies were found to be positive and proteins C, S were found to be low. This confirmed the diagnosis of APLA. Patient was subsequently initiated on tab rivoraxaban and was discharged.

### Key words

Antiphospholipid antibody, Portal vein thrombosis, SMV thrombosis.

## Eaton Embolism – A Case Report On Mycoplasma Pneumonia

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Chettinad Health City Medical Journal 2019; 8(2): 86

### Abstract

Community acquired pneumonia causing pulmonary embolism is known as infarction pneumonia. The term "Eaton agent" refers to mycoplasma pneumonia which in this case has lead to pulmonary embolism hence the title Eaton Embolism. A 27 year old female came with complaints of high grade fever, productive cough, and breathlessness for one week. On examination patient was found to be tachypnoeic with type 1 respiratory failure. Chest xray showed bilateral non homogeneous opacity suggestive of ARDS. Echo revealed moderate PAH. HRCT revealed bilateral segmental and sub segmental pulmonary artery thrombosis with features suggestive of bilateral consolidation and pleural effusion. Lower limb venous doppler was normal. Coombs test was positive with positive mycoplasma serology. ANA, Anti beta2 microglobulin were positive and dsDNA was negative. In view of worsening ARDS, patient was intubated following a trial with NIV. Patient was started on broad spectrum antibiotic (meropenam and clarithromycin) along with anticoagulants and steroids in view of vasculitis picture. Patient significantly improved with treatment and discharged with oral anticoagulants and steroids.

### Key words

Pulmonary embolism, Mycoplasma Pneumonia, Coombs test, Anti beta2 microglobulin.

## A Case Of Acute Methyl Salicylic Acid Poisoning

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Chettinad Health City Medical Journal 2019; 8(2): 87

### Abstract

Methyl salicylate contains a higher quantity of salicylic acid than any other compound. This is found in extremely high concentrations in oil of winter green. Both oral and local exposure can result in systemic symptoms, particularly multiple acid base disturbances, dyselectrolytemia, respiratory failure and CNS manifestations of varied proportions. The management is primarily supportive with no definitive antidote. Here we report a case of accidental oil of wintergreen poisoning, at the maximal lethal dose, in a middle aged female with a detailed reporting on the clinical background, varied acid base changes, the derangement in various metabolic parameters not limited to the LFT, and the response of the patient to multiple cycles of forced alkaline diuresis and haemodialysis. The patient succumbed to respiratory failure within 72 hours, despite appropriate protocol being followed in the treatment. This case scenario has revealed much about methyl salicylic acid poisoning, which is generally rare to encounter in the Southern States.

### Key words

Methyl Salicylate, Dyselectrolytemia, Respiratory failure, Lethal dose.

## An Uncommon Presentation Of Acute Aortic Dissection

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Chettinad Health City Medical Journal 2019; 8(2): 87

### Abstract

A 43 year old male who is a known hypertensive on treatment for the past 10 years presented to our hospital with complaints of dry cough for three weeks and one episode of syncope on the morning of presentation. He had no history of chest pain, dyspnoea or palpitations. On examination he had bounding carotid pulsations with pulse rate of 100 per min, regular, collapsing in nature. His blood pressure was 180/90 mm Hg (right upper limb). Cardiovascular examination revealed an early diastolic murmur of grade 3. Other systems were normal on examination. A chest x- ray revealed mediastinal widening. ECG showed sinus tachycardia, 2D echocardiography showed dilated aortic root (6.5 cm), dissection flap involving the ascending aorta, severe aortic regurgitation with a central jet, left ventricular hypertrophy with adequate ejection fraction. Subsequently patient was taken up for a CT aortogram and confirmed to have type A acute aortic dissection. He was promptly taken up by the cardiothoracic team for an emergency Bentall procedure with aortic valve replacement. He recovered and was discharged 1 week after the procedure.

### Key words

Acute aortic dissection, Bentall procedure, Mediastinal widening

## Stress Induced Cardiomyopathy

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Chettinad Health City Medical Journal 2019; 8(2): 88

### Abstract

Stress induced cardiomyopathy also known as Takotsubo syndrome, Broken heart syndrome, Happy heart syndrome or Apical ballooning syndrome was first described in Japan in 1991. It was named after the tako-tsubo, which is an Octopus trap, the shape of which is similar to LV apical ballooning. It accounts for 1-2% of suspected acute coronary syndrome, more (90%) in post menopausal women. Triggering factors are emotional, physical or combined. Catecholamine excess, coronary spasm, microvascular dysfunction and myocarditis are the underlying pathophysiological mechanisms. Chest pain, dyspnea, syncope and rarely shock will be the presentation. ECG may reveal ST elevation in chest leads, ST depression or isolated T wave inversion along with elevated troponin. Echocardiographic findings are LV apical ballooning, mid ventricular hypokinesia, global hypokinesia or focal hypokinesia. Coronary angiogram will reveal normal coronary arteries. Heart failure, cardiogenic shock, LVOT obstruction, mitral valve dysfunction, thromboembolism and death are the complications. Beta-blockers, antiplatelets, ACEI, are useful. Prognosis is usually good. ECG and ECHO findings revert to normal over days to weeks. We analysed the prevalence of stress induced cardiomyopathy among 1360 ACS patients from August 2018 to June 2019 and the incidence was 1.09%. with M:F 1:4. Our other observations correlate with the literature.

### Key words

Stress induced cardiomyopathy, Apical ballooning with hypokinesia, Chest pain

## Is It Autoimmune Polyglandular Syndrome?

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Chettinad Health City Medical Journal 2019; 8(2): 88

### Abstract

Autoimmune polyglandular syndrome (APS) comprises a diverse group of clinical entities involving functional impairment of multiple endocrine glands. We present a 36 year old female, who presented with weakness of bilateral lower limbs and drooping of eyelids which worsened over the day. Neurological examination showed bilateral ptosis with bilaterally exaggerated deep tendon reflexes and fine tremors involving both hands. A clinical possibility of myasthenia gravis along with hyperthyroidism was considered. Repetitive nerve stimulation showed a decremental response consistent with myasthenia gravis. Thyroid profile showed elevated free T4, reduced TSH and elevated anti TPO antibody titres. Imaging showed bilateral enlarged polycystic ovaries. We have to consider the possibility of APS when patient present with 2 or more autoimmune disorders. Long term follow up is needed to look for the development of other manifestations of APS.

### Key words

Myasthenia Gravis, Thyroid Disorders, Autoimmune Polyglandular Syndrome

## Hashimotos Thyroiditis Presenting As Intractable Hiccup

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Chettinad Health City Medical Journal 2019; 8(2): 89

### Abstract

Hiccup is an involuntary, intermittent, spasmodic contraction of the diaphragm and intercostal muscles with sudden inspiration that ends with abrupt closure of the glottis, usually transient. Hiccup lasting longer than 48 hours are persistent and those lasting more than 2 months are intractable hiccups. Chronic persistent hiccups are usually due to renal, cardiac, neurological and gastrointestinal causes. Hiccup is common in clinical practice but rarely seen after introduction of H<sub>2</sub> receptor blocker and PPIs. Hiccup has been reported rarely as a symptom in patients with hyperthyroidism and not reported in hypothyroidism so far. Hashimoto's thyroiditis is a chronic lymphocytic thyroiditis of autoimmune origin common between 40-65 years in females and rare in males. Here we report a case of 40 year old male with chronic persistent intractable hiccup as presenting symptom of hypothyroidism in Hashimoto's thyroiditis. The possible mechanism being intrathyroidal inflammation causing stimulation and irritation of phrenic nerve. Rarely hiccup has been discussed in ward rounds and mechanisms are not recalled frequently.

### Key words

Hiccup, Hashimoto's thyroiditis, Hypothyroidism

## Cerebral Fat Embolism

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Chettinad Health City Medical Journal 2019; 8(2): 89

### Abstract

Fat embolism syndrome is a rare but serious clinical manifestation occurring after traumatic injury to long bones. Only 3-10% of long bone fracture patients develop clinical manifestations of the syndrome. Classical triad of cerebral, respiratory and cutaneous manifestations may not be present in all. A 58 year old male with alleged history of trauma to bilateral lower presented with altered sensorium. There was no history of head injury. CT brain was normal, CT pulmonary angiogram revealed no thrombosis. 2D ECHO showed no evidence of patent foramen ovale. MRI Brain revealed multiple acute infarcts suggestive of fat embolism. Cerebral fat embolism occurs by 2 mechanisms. First, fat globules enter the left atrium from the right heart through a shunt patent foramen ovale. Second, it may filter directly through the lung capillaries to reach the arterial system. Microemboli are small and malleable and may not lead to significant pulmonary injury. Cerebral fat embolism is a clinical diagnosis, but specific findings on neuroimaging studies are strongly supportive.

### Key words

Cerebral fat embolism, Patent foramen ovale, Lower limb injury

## An Interesting Case Of CIDP Associated With Leucoclastic Vasculitis And Hemolytic Anemia

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### Abstract

Chronic inflammatory demyelinating polyneuropathy (CIDP) is characterized by progressive weakness and impaired sensory function in the legs and arms. It is caused by damage to the myelin sheath of the peripheral nerves. CIDP is closely related to Guillain-Barre syndrome and it is considered the chronic counterpart of that acute disease. Leukocytoclastic vasculitis is characterized by nuclear debris from the neutrophils that have infiltrated in and around the vessels during acute stages. Erythrocytes often extravasate from the involved vessels, leading to palpable purpura. We report a case of 68 year old male who is a known case of chronic inflammatory demyelinating polyneuropathy for 20 years, now presented with complaints of bilateral lower limb swelling, decreased urine output, hematuria, easy fatigability and dyspnoea on moderate exertion. On examination patient was pale with bilateral pitting pedal edema. He had hyperpigmented maculopapular skin lesions all over the body associated with severe burning sensation, severe myalgia, and bilateral wrist joint pain. Skin biopsy confirmed IgA negative leucocytoclastic vasculitis.

### Key words

Chronic inflammatory demyelinating polyneuropathy, Leucocytoclastic vasculitis.

## An Interesting Case Of High SAAG Ascitis

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Chettinad Health City Medical Journal 2019; 8(2): 90

### Abstract

We present a case of hypothyroidism, who presented with abdominal distention, breathlessness and pedal edema. Patient had history of diabetes, hypertension, and coronary artery disease. Patient was on thyroxine 100mcg, but was still having low serum thyroid hormone levels (serum T<sub>3</sub> was 1.68pg/ml, serum T<sub>4</sub> was 0.81ng/dl and TSH was 25.26 IU). Analysis of ascitic fluid revealed high SAAG, high protein ascites. We followed the algorithm and our case was not fitting into any of the causes for high SAAG ascites. By exclusion, we diagnosed hypothyroidism as cause for ascites in this case. Ascites is usually seen in liver cirrhosis, hepatic venous outflow or portal vein or IVC obstruction, CCF, nephrotic syndrome, malignancy, any infection and pancreatitis. Massive ascites is a very rare presentation in hypothyroidism. They require therapeutic ascitic tapping and correction of thyroid level is the definitive treatment which will prevent recurrence.

### Key words

Hypothyroidism, Abdominal distention, Massive ascitis, High SAAG.

## A Rare Presentation of Cerebello Pontine Angle Tumor

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### Abstract

Cerebello pontine angle is the most common location of posterior fossa tumor. The most common CP angle tumor is vestibular schwannoma accounting for 85%-90%, followed by meningiomas. The clinical features vary according to the site and mass effect by the tumor. We report a 50 year old male patient who presented with intermittent tinnitus, vertigo and syncope after an assault (blunt injury) to head 10 days ago. On examination he was found to have decreased sensation over the left side of the face. He had absent corneal reflex and sensory neural hearing loss on left side. MRI brain showed T1 hypointense lesion involving VIIth and VIIIth nerve complex in left cerebellopontine angle region.

### Key words

Syncope, Tinnitus, Corneal reflex, Cerebello pontine angle

## All Cherries Are Not Sweet – A Case of Central Retinal Artery Occlusion

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### Abstract

Central retinal artery occlusion (CRAO) presents with acute painless loss of monocular vision. It is considered as a form of stroke with same clinical approach and management. Incidence is 1 to 10 per 100,000 people. We report a 59 year old male, a known case of type 2 diabetes mellitus and hypertension who presented with chest pain and breathlessness. He was initially treated conservatively for NSTEMI and developed sudden onset of loss of vision in left eye on the next day. On examination, left eye showed no perception of light with relative afferent pupillary defect. Fundus examination revealed bilateral non proliferative diabetic retinopathy with cherry red spot in left eye. MRI brain showed acute infarct in left mammillary body, left half of optic chiasma and canalicular segment of the left optic nerve, and thrombotic occlusion of the intracranial segment of the left internal carotid artery. Carotid Doppler showed eccentric soft plaque in the right common carotid artery, left ICA causing moderate luminal narrowing, patchy flow at the origin of the left ICA with absent flow in the remaining visualized ICA. He was treated with dual antiplatelets and insulin. CRAO patients are at risk of subsequent cardiovascular as well cerebrovascular events with reduced life expectancy. Unless the etiology is known at presentation, carotid artery imaging study is recommended for all patients with CRAO.

### Key words

Central Retinal Artery Occlusion, Cherry Red Spot, Coronary Artery Disease

## An Unusual Cause Of Sensorineural Hearing Loss

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Chettinad Health City Medical Journal 2019; 8(2): 92

### Abstract

A 27 years old male presented with bilateral hearing difficulty for the past 10years. Recently patient reported worsening of hearing loss for last two weeks. Cranial nerve examination revealed bilateral sensory neural hearing loss. On evaluation he was found to have raised haemoglobin levels. He was a smoker for eight years and smokes approximately one pack per day. His serum erythropoietin levels were high and JAK 2 mutation was negative. In view of elevated erythropoietin and negative JAK-2 mutation possibility of secondary polycythemia was considered. Hence three cycles of phlebotomy was done. Patient's hearing improved after three cycles of phlebotomy.

### Key words

Sensory neural hearing loss, Secondary polycythemia, Phlebotomy.

### Image Answer



Copenhagen Denmark : \* The concept of intensive care unit emerged here



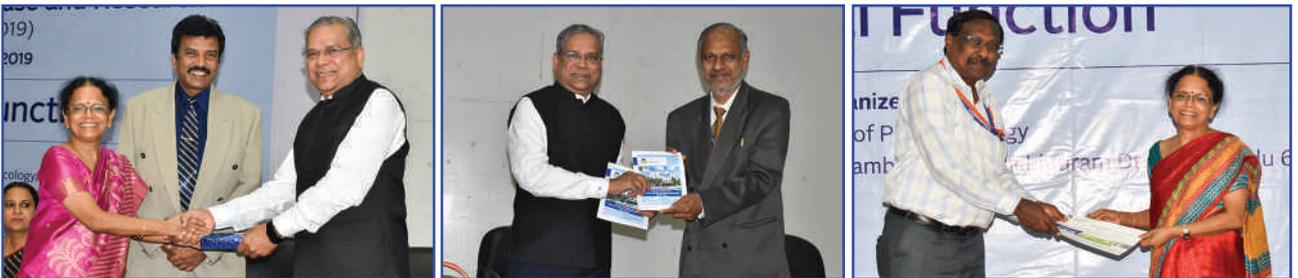
Initiator of world's first multidisciplinary intensive care unit-Björn Ibsen December 1953, Copenhagen Denmark during polio epidemic.  
PC. <https://www.researchgate.net>



A medical student manually ventilating young girl with poliomyelitis (Copenhagen, 1953)  
PC. <https://www.semanticscholar.org>

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M.Sc. Health & Yoga

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M.Sc.(AHS) Radiology and Imaging Science Technology

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M.Sc. Renal Dialysis Technology

M.Sc. Respiratory Care Technology

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Bachelor of Economics (3 Years)

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