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*MEDICAL DIARY*

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# Contents

**Editorial**

- **Editorial** 2  
*Dr. Jane CK CHAN*

**Education Bulletin**

- **Adult Respiratory Distress Syndrome: Challenges and Triumphs** 5  
*Dr. Donald YC YU*  
*Dr. Jane CK CHAN*
- **MCHK CME Programme Self-assessment Questions** 10
- **Update of Renal Replacement Therapy in the ICU** 13  
*Dr. Wing-wa YAN*
- **Molecular Adsorbents Recirculating System (MARS): Evidence and Management Pitfalls** 19  
*Prof. Sheung-tat FAN*  
*Dr. Alexander CHIU*
- **Mechanical Circulatory Support in the Intensive Care Unit** 23  
*Dr. Elaine MC CHAU*  
*Dr. Tak-fu TSE*
- **Infectious Disease Emergencies** 29  
*Dr. Samson SY WONG*  
*Dr. Vincent CC CHENG*

**Drug Review**

- **Sedation and Analgesia in the Intensive Care Unit** 31  
*Dr. Judith SHEN*

**Life Style**

- **Scuba Diving** 35  
*Dr. Gloria PEI*

**Dermatological Quiz**

- **Dermatological Quiz** 36  
*Dr. Lai-yin CHONG*

**Society News** 30**Federation News** 40**Medical Diary of September** 37**Calendar of Events**

- **Meetings** 39
- **Courses** 39



## Editorial

### Dr. Jane CK CHAN

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*Specialist in Respiratory Medicine*

#### Editor



Dr. Jane CK CHAN

This September issue of the Hong Kong Medical Diary on Intensive Care represents the very first time the Medical Diary has incorporated Intensive Care into the list of medical topics to be shared with Diary readers. The breadth of mind of the Diary Editors for entertaining non-traditional medical subjects such as Intensive Care and the boldness in committing one whole issue to this subject are much to be congratulated on for making this issue possible. Much gratitude goes to the current and former Editors-in-Chief, Drs Chun-on Mok and Walter King, for their kind encouragement and support. Much gratitude also goes to the esteemed authors of this issue, who, based on their vast experience in managing the critically ill in the intensive care unit (ICU), have together produced this very handsome issue on Intensive Care.

Indeed the timing for the birth of this issue on Intensive Care is just right. For a few decades after the initial development of negative pressure ventilators (or so-called iron lung) to support patients with respiratory failure during the polio epidemic, the ICU had remained a rather humble shapeless place, usually serving as a post-operative recovery area, or as a pooled nondescript repository for nursing ill patients requiring various vital organ monitoring and support. Over the past two-plus decades, the explosion in our knowledge and understanding of the pathophysiology of the critically ill, along with the vast technological advances and increasing practice of evidence-based medicine, has enabled the modern-day ICU to provide much more meticulous and well-contemplated ICU care targeting not only at saving lives but also at minimising iatrogenesis. In this issue, we are proud to present updates on acute renal support (by Dr. W. W. Yan), on acute liver support (by Dr. Alex Chiu and Prof S. T. Fan), on acute cardiac support (by Drs T. F. Tse and Elaine Chau), on infectious disease emergencies commonly seen in the ICU (by Drs. Vincent Cheng and Samson Wong), on optimising sedation and analgesia (by Dr. Judith Shen), and on respiratory support (by Dr. Donald Yu and myself). This issue thus provides a bird's eye view of the fast expanding global literature and experience in Intensive Care.

This issue inevitably suffers some important omissions because of limited space. Sepsis, a common ICU entity, is not discussed here. For an evidence-based update on sepsis, our readers are encouraged to look up the website [www.survivingsepsis.org](http://www.survivingsepsis.org) recently established jointly by the European Society of Intensive Care Medicine, the International Sepsis Forum and the U.S.-

based Society of Critical Care Medicine. The annual edition of *The Yearbook of Intensive Care and Emergency Medicine* edited by J.-L. Vincent, Professor and Head of a leading Intensive Care Department in Europe is another must-read source for those who would like to sample the amazing progress made in Intensive Care over the years.

To match up to the artistic photography of the past issues was a challenging task for me as an issue editor on Intensive Care, as the prototype image of Intensive Care can be frightening and intimidating: a patient lying helplessly in bed with tubes and lines and machines of various sizes and shapes hovering at the bedside. Fortunately, Professor Richard Yu has kindly graced our cover with the beauty of a snowy winter. Many paradoxical emotions indeed come to mind when one considers the ICU, such as hope/despair or aggressive intervention/end of life. Nonetheless, the beauty of the ICU lies in the fact that this is the place where the sanctity of life is stretched to its farthest limits, where timely appropriate therapeutic interventions and organ support do matter, and where life tragedies and miracles can be seen together. That is the challenge of Intensive Care, and that is why Intensive Care can be a passion for someone like myself since my earlier days as the Director of the ICU at Queen Mary Hospital.

This issue probably breaks the Medical Diary's record in two other ways. Firstly, mirroring the Intensive Care multi-disciplinary practice, our authorship comprises of experts from many specialties. On board our authorship team are physicians, an anaesthetist and a surgeon; there are specialists in Cardiology, Critical Care Medicine/Intensive Care Medicine, Hepatobiliary Surgery, Clinical Microbiology & Infection, and Respiratory Medicine. Mirroring the important bedside collaboration in the ICU, our multi-disciplinary team of authors have joined hands in the delivery of this issue to you. Secondly, the Life Style article contributed by Dr Gloria Pei would likely be a first in depicting the power of a mother's love for her little one, a truly heart-warming story.

Lastly, may I wish the Hong Kong Medical Diary every success and our readers good health and happiness!



## The Cover Shot



Early winter when the first snow fell after X'mas in Erabandai in Fukushima, the image captured the serenity and tranquility of nature and its purity.

This photo impressionism is shared with Dr. Leo KK Wong who is my mentor and teacher.



**Prof. Richard YH YU**

MD(HK), PhD(Lond), FRCP,  
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6 October 2009	Mechanical ventilation (i) Principles and practices (ii) Tracheostomy care	Dr. Chun-Wing LAU 劉俊穎醫生 Ms. Yuen-Ping LAM 藍婉平女士
13 October 2009	Influenza (i) An update including human swine influenza (ii) Infection control	Dr. Wai-Cho YU 余衛祖醫生 Ms. Wai-Chun TANG 鄧慧珍女士
* 20 October 2009	Non-pharmacological treatment of COPD (i) Pulmonary rehabilitation (ii) Smoking cessation	Dr. Thomas MOK 莫恩榮醫生 Ms. Doris TSE 謝笑芬女士
27 October 2009	(i) Postoperative respiratory failure (ii) Deep vein thrombosis and pulmonary embolism	Dr. Wai-Ming CHAN 陳惠明醫生

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#### References:

1. AmBisome, Summary of Product Characteristics, 5 July 2007.
2. Cornely O et al. Clin Infect Dis 2007; **44**: 1289-97.
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## Adult Respiratory Distress Syndrome: Challenges and Triumphs

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 September 2009.

## Case Presentation

### Patient 1. A young woman with rheumatoid arthritis and acute respiratory failure

#### Background

A 33 year-old obese Chinese female, nonsmoker, with longstanding history of rheumatoid arthritis (RA) since childhood sequentially requiring systemic steroids, penicillamine, oral gold, plaquenil, and 4 years earlier, leflunomide (Arava®), was admitted directly to the ICU for acute onset of high fever and oxygenation failure. There had been a prodrome of fever, nonproductive cough, shortness of breath, vomiting and diarrhoea for a few days prior to admission. Her chest examination revealed diffuse crepitations throughout both lungs.

#### Investigations

Her chest x-ray on admission showed bilateral diffuse consolidative changes (Figure 1A). Her white cell count was  $1.72 \times 10^9/L$  with total neutrophil count of  $1.31 \times 10^9/L$  and lymphocyte of  $0.25 \times 10^9/L$ . The platelet count was  $107 \times 10^9/L$ . Her CRP, procalcitonin and renal function tests were all normal. Her liver function tests were normal except for a SGOT of 109 U/l. The ESR was 35 mm/h. A subsequent chest CT showed extensive ground glass consolidation in both lungs sparing only the dorsal and apical regions consistent with acute pneumonitis (Figure 1B). The working diagnosis was fulminant community-acquired pneumonia versus leflunomide-induced interstitial pneumonitis. Leflunomide was promptly discontinued. Cholestyramine was given to accelerate the clearance of leflunomide.

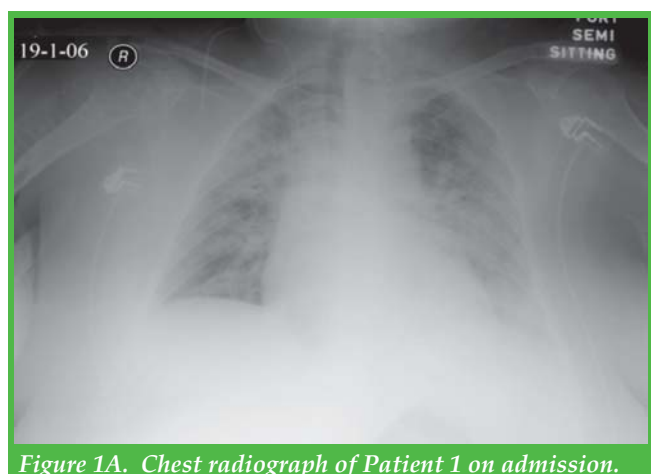


Figure 1A. Chest radiograph of Patient 1 on admission.

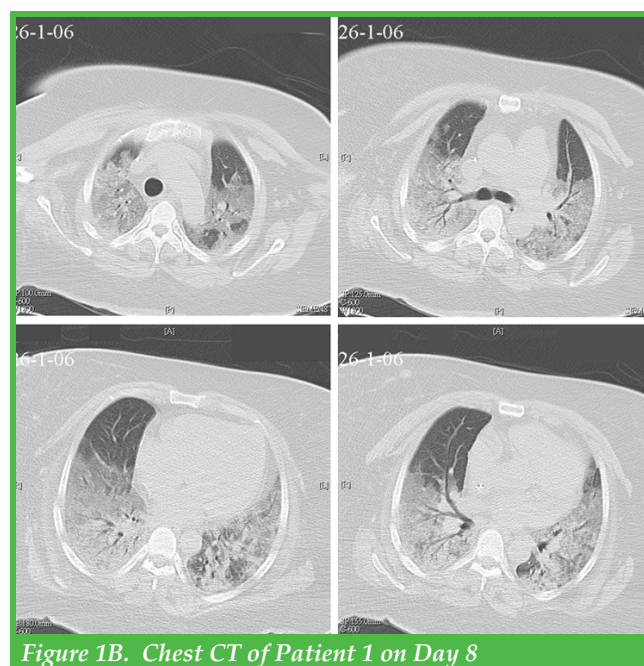


Figure 1B. Chest CT of Patient 1 on Day 8

#### Workup for Infection

She was pan-cultured on admission for high fever and was promptly started on broad-spectrum antibiotics including a beta-lactam, a macrolide, and anti-PCP and anti-fungal therapy based on microbiology consultation. She developed an episode of hypotension on **Day 3**, for which stress dose steroids and intravenous immunoglobulin were added for possible fulminant sepsis. One dose of G-CSF was given on **Day 4** for persistent leukopenia, followed by good sustained recovery of her white cell count in the ensuing days. The lymphopenia persisted till **Day 11**. All microbiologic workup turned out to be negative: sputum and blood cultures, sputum for acid fast bacilli smear and PCR, urinary antigen for Legionella and Streptococcus, serologic titres for mycoplasma, nasopharyngeal aspirate for influenza A and B, and serum CMV pp65. All her immune markers were also negative.

#### Stormy Course in Respiratory Support

The patient required BIPAP support on **Day 1** immediately upon ICU admission because of poor oxygenation. A  $FIO_2$  of 50% on BIPAP could achieve an oxygen saturation ( $SpO_2$ ) of 80-85% only. Over the following week, her oxygenation remained very

marginal with SpO<sub>2</sub> achievable above 90% at FIO<sub>2</sub> of  $\geq 70\%$ . Mild exertion or coughing would precipitate marked oxygen desaturation down to 70s%. **On Day 11**, as the patient's oxygenation deteriorated despite being on BIPAP, with SpO<sub>2</sub> barely above 90% on FIO<sub>2</sub> 80%, the patient was intubated and tracheostomy was performed. Ventilatory support showed a PEEP level of 15 cm together with a FIO<sub>2</sub> of about 60% to achieve a SpO<sub>2</sub> of 90-91%. **On Day 18**, the patient was commenced on bi-level ventilation for her fulminant ARDS with severe oxygenation failure.

### *Empiric Corticosteroids*

The patient's fever peaked on **Day 2** but gradually came down (possibly from stress dose steroids) over the next few days and henceforth remained afebrile. **On Day 9**, in view of the totally negative microbiologic workup, multi-system presentation, leukopenia, lymphopenia, and the diffuse pneumonitis, the diagnosis of leflunomide-induced ARDS was felt to be likely. Pulse steroids in the form of daily methylprednisolone 500 mg for 2 days was given for the worsening respiratory failure and fulminant ARDS, followed by pharmacologic doses of steroids with gradual tapering over the next few weeks.

### *Inhaled Nitric Oxide*

**On Day 22**, a repeat CT scan of the chest showed worsening ground glass consolidation with reticular shadows consistent with evolving pneumonitis. **On Day 23**, in view of the patient's worsening oxygenation failure requiring FIO<sub>2</sub> of 85%, inhaled nitric oxide (iNO) was initiated to enhance gas exchange and for fear of oxygen toxicity. iNO at 5 parts per million (ppm) was administered via the InoVent. Within 12 hours of iNO administration, the patient demonstrated pleasing response with improvement in the SpO<sub>2</sub> thus enabling tapering down of FIO<sub>2</sub>. By **Day 25**, the patient's FIO<sub>2</sub> came down to as low as 50-55%. iNO was brought down gradually to 1 ppm and eventually off after a total course of 6 days. FIO<sub>2</sub> requirements remained stable off iNO. **On Day 34**, the FIO<sub>2</sub> requirements were 35-40% only. **On Day 38**, a repeat CT chest showed partial resolution of the alveolar process and lessening of the interstitial reticular markings.

### *The Road to Recovery*

Her clinical course was otherwise only complicated by Klebsiella-related ventilator-associated pneumonia which responded to prolonged course of antibiotics. **On Day 40**, the patient was switched from IV steroids to oral prednisolone at 60 mg qd. By **Day 45** she was able to sustain spontaneous breathing most of the day. By **Day 55**, the patient was completely off the ventilator, and was soon discharged from the ICU. The patient finally went home after a hospital stay of 3 months.

### *Final Diagnosis*

Leflunomide-induced ARDS

## **Patient 2. An elderly woman with acute respiratory failure following VATS lung biopsy**

### *Background*

A 78 year-old Chinese female, nonsmoker, with history of hypertension and paroxysmal atrial fibrillation on warfarin and amiodarone (Cordarone®) 100 mg bd, was electively admitted to the hospital for wedge lung

biopsy under video-assisted thoracoscopy. There had been a history of insidious onset of exertional dyspnoea and recent chest x-ray and CT finding of bibasilar subpleural infiltrates more on the left than right, with some suggestion of honeycomb lung in the left base (Figure 2A and 2B). Pre-operative myocardial perfusion scan was normal, and so were her chest examination and resting oximetry reading. VATS wedge biopsy of the left lower lobe was performed on **Day 2**. Intra-operatively, pleural fibrosis and lung nodularity were noted on palpation. Histology of the resected lung showed interstitial fibrosis with chronic inflammatory infiltrate consistent with usual interstitial pneumonitis. All stains for micro-organisms were negative.



Figure 2A: Chest radiograph of Patient 2 nine days before admission



Figure 2C: Chest radiograph of Patient 2 two days following VATS lung biopsy



Figure 2B: Chest CT of Patient 2 five days before admission

### *Fulminant ARDS Postoperatively*

One day following wedge lung resection (**Day 3**), the patient developed low grade fever, for which antibiotics were empirically started. **On Day 4**, she was noted to have oxygen desaturation which rapidly progressed to require BIPAP support at FIO<sub>2</sub> of 65%. Auscultation revealed a few bi-basilar crepitations. Chest x-ray showed interval development of extensive airspace consolidation in both lungs, most prominent at both





lower zones. (Figure 2C) In view of the rapidly deteriorating condition and likely non-infectious pneumonitis, the patient was given pulse steroids in the form of methylprednisolone 500 mg qd for 3 days from **Day 4 through Day 6** followed by prednisolone 50 mg qd beginning on **Day 7**. Diuretics were also given for possible fluid overload. From **Day 7 through Day 9**, the patient was put on spontaneous breathing with oxygen at 8 L+30%, achieving rather marginal O<sub>2</sub> saturation of 90-94%. On **Day 10**, the patient appeared rather fatigued and tachypnoeic with a respiratory rate of 40, and required resumption of BIPAP. On **Day 11**, she was transferred to the ICU for intubation and invasive ventilation using PEEP levels of 10 cm H<sub>2</sub>O and FIO<sub>2</sub> of 85%. However, her oxygenation failure remained profound requiring bi-level ventilation and FIO<sub>2</sub> up to 100%. A bronchoalveolar lavage did not reveal any infectious aetiology for her oxygenation failure. Serum immune markers were normal. The working diagnosis was fulminant ARDS secondary to acute and chronic lung injury from amiodarone. Amiodarone was discontinued.

### *Empiric Treatment of Amiodarone-induced ARDS*

High dose steroids were continued. Oxygen radical scavenger therapy was started using vitamin C, vitamin E, pentoxylline, and N-acetylcysteine. One dose of anti-tumour necrosis factor-alpha antibody was also given for possible cytokine storm associated with the acute lung injury. By **Day 13**, FIO<sub>2</sub> requirement came down to 75%-85% at a PEEP level of 10 maintaining a SpO<sub>2</sub> of 91%, by **Day 15** FIO<sub>2</sub> down to 55% with a SpO<sub>2</sub> of 92%, and **Day 16** FIO<sub>2</sub> down to 45% with a SpO<sub>2</sub> of 91-92%, consistent with encouraging clinical response. However, she continued to demonstrate heightened respiratory drive with persistent tachypnoea up to 40 and marked use of accessory muscles despite full ventilatory support and generous doses of sedation. Her ICU course was further complicated by rather difficult-to-control atrial fibrillation, subcutaneous emphysema, right pneumothorax, steroid-induced diabetes, and critical illness polyneuropathy. The patient was eventually off the ventilator on **Day 30**, discharged from ICU on **Day 34**, and discharged home on **Day 78**.

### *Final Diagnosis*

Amiodarone-induced ARDS

## Discussion

### *Definition of ARDS*

The acute respiratory distress syndrome (ARDS), first described in 1967<sup>1</sup>, is characterised by diffuse inflammation of the lung's alveolar-capillary membrane in response to various pulmonary and extra-pulmonary insults<sup>2</sup> such as aspiration, pneumonia, sepsis, trauma, or pancreatitis. The 1994 American-European consensus<sup>3</sup> on the definition of ARDS is acute onset of

- (1) Hypoxaemia, with a PaO<sub>2</sub>/FIO<sub>2</sub> ratio of 200 mmHg or less,
- (2) Bilateral infiltrates on a frontal chest radiograph, and
- (3) Pulmonary artery wedge pressure < 18 mmHg or no clinical evidence of left atrial hypertension.

Patients with ARDS invariably require mechanical

ventilation and prolonged ICU stay. Mortality rates remain high at 35-60%<sup>2</sup>. Management strategies for ARDS have focused on combating the inciting insult, ventilatory optimisation and at times cautious use of steroids.

### *Drug-induced ARDS*

Drug-induced lung diseases can manifest in various clinico-pathological entities as shown in Table 1, based on the cellular mechanism of lung injury as well as the tempo of disease presentation, ranging from slowly progressive pneumonitis/fibrosis to acute respiratory failure arising from either diffuse alveolar damage (DAD), non-cardiogenic pulmonary oedema or alveolar haemorrhage<sup>4,5</sup>. The aetiologic link to a certain drug can be difficult, and is usually based on a history of drug exposure, histological evidence of lung damage, and exclusion of other causes of lung injury, especially the exclusion of active infection. In the milder cases, radiographic findings of subtle ground glass opacities and mild fibrosis can be elusive on conventional chest x-ray and may only be seen on CT scanning<sup>5</sup>.

Despite our clinical impression to the contrary, noncardiogenic pulmonary oedema, and to lesser extent, ARDS, are common clinical manifestations of drug-induced lung diseases<sup>6</sup>. The former can be mild and self-limited, with rapid recovery following the use of oxygen and diuretic therapy, and discontinuation of the culprit drug. However, the more severe form, usually presenting as fulminant ARDS, as resulting from Ara-C, nitrofurantoin, or amiodarone, can be life-threatening and may require ventilatory support and administration of steroids<sup>6</sup>. Drug-induced ARDS is by and large a diagnosis by exclusion; every effort has to be made to exclude other important causes of ARDS, including sepsis, fulminant pneumonia and aspiration.

### *Leflunomide-induced ARDS*

Leflunomide (Arava®) is a disease-modifying anti-rheumatic drug for the treatment of rheumatoid arthritis (RA). The drug had been considered relatively safe for quite a few years since its launch in the U.S. and E.U. in the late 1990s, with common adverse events being nausea, diarrhoea, headache, deranged liver enzymes, rash, alopecia, respiratory infections and hypertension<sup>7</sup>.

However, within a few months after its release in Japan in September 2003, 48 cases of interstitial lung disease (ILD) were found among 4395 patients registered for use in Japan, including 16 fatal cases, giving rise to an incidence of 1.1%, and a fatality of 30%<sup>8</sup>. A stormy course of acute respiratory failure from leflunomide leading to fatality was described despite the use of high dose steroids<sup>9,10</sup>. Pathological findings at autopsy were that of DAD<sup>9</sup>. DAD manifested as widespread patchy ground glass opacities and/or consolidation also appeared to be the predominant presenting finding radiographically<sup>11</sup>.

There does appear to be a difference in the susceptibility to leflunomide-induced lung toxicity between different ethnic/geographic groups. Subsequent to the Japanese findings, Canadian investigators conducted a retrospective population-based case control epidemiologic study reviewing more than 60,000 Canadian patients with RA on leflunomide between 1998 and 2003 and found a much lower rate of leflunomide-



induced ILD, with the hospitalisation rate for ILD being 8.1 per 10,000 per year (0.08%)<sup>12</sup>. This discrepancy between Japan and the western countries in the incidence of lung toxicity was also tacitly echoed in a consensus statement written by a multi-disciplinary panel of rheumatologists and general practitioners across the U.K. in late 2004. The consensus statement, published in early 2005, amidst the publicity aroused by the Japanese clinicians/investigators, did not include lung toxicity on their list of adverse events<sup>13</sup>.

A recent multivariate logistic regression risk analysis of the large Japanese registry revealed the following risk factors for leflunomide-induced lung injury: preexisting ILD, with odds ratio (OR) of 8.17, loading dose administration (OR 3.97), smoking history (OR 3.12) and low body weight (OR 2.91)<sup>14</sup>. Fatality was most observed in those with severe hypoxaemia requiring mechanical ventilation, high C-reactive protein level, hypoalbuminaemia, and persistent lymphopenia<sup>14</sup>. Nevertheless, *de novo* cases of leflunomide-induced lung injury in the absence of the above-mentioned risk factors do occur, as in our patient (Patient 1) and as reported in the literature<sup>12</sup>.

Current Japanese recommendation places leflunomide as a second-line drug not to be used in smokers, or those with low body weight or with preexisting ILD. Loading dose should not be given<sup>14</sup>. Careful monitoring for drug toxicity is warranted, and when lung injury develops, accelerated drug elimination using cholestyramine and early use of steroids constitute the mainstay of treatment<sup>8</sup>.

### ***Amiodarone-induced ARDS***

The pulmonary toxicity associated with amiodarone therapy is a major factor limiting the widespread use of this very effective anti-arrhythmic agent. Amiodarone-induced lung disease occurs in about 5-10% of patients receiving the drug<sup>15</sup>, manifesting itself in the form of subacute onset of dyspnoea and CT findings of diffuse interstitial thickening (known as subacute interstitial pneumonitis or fibrosis), or as nodular areas of subpleural consolidation with histological features of bronchiolitis obliterans organising pneumonia, or as acute onset of dyspnoea and fever with CT findings of dependent consolidation typical of ARDS<sup>16</sup>.

The pharmacokinetic properties of amiodarone predispose the lung to amiodarone toxicity. Firstly, amiodarone is lipophilic with a large volume of distribution, hence the long elimination half-life at 45-60 days and likely storage in organs with high lipid content such as fat, lung and liver<sup>15</sup>. Secondly, amiodarone's principal metabolite, desethylamiodarone, accumulates in peripheral tissues providing a sustained reservoir, to the extent that concentrations measured in unfractionated lung parenchyma significantly exceed that of the heart, setting up the lungs up for toxic effects of amiodarone<sup>17</sup>.

Mechanisms underlying lung toxicity have been poorly understood, likely because of the heterogeneity of amiodarone lung syndromes and corresponding histopathological findings. Two prevalent hypotheses have been (1) adaptative-immune-mediated hypersensitivity reaction based on findings of an

inflammatory response similar to inhalation of organic dust<sup>15</sup>, and (2) direct drug-induced phospholipidosis<sup>17</sup>, arising from a direct toxic effect of the drug, and characterised by the histopathological findings of "foamy" changes in the alveolar macrophages<sup>15</sup>. The role of free radicals in the pathogenesis of amiodarone toxicity was further implicated in *in vitro* and *in vivo* models of amiodarone lung<sup>15,18</sup>.

However, beginning in the mid-to-late 1980s, it became increasingly apparent that the mechanism of lung injury may differ between chronic amiodarone lung disease and acute amiodarone-mediated lung injury. In the former, risk groups have been identified as those who are elderly with pre-existing lung condition on doses of > 400 mg per day<sup>17</sup>. In the latter, which usually presents as an acute and rapidly deteriorating, and at times fatal, illness, the risk factors revolve around concomitant injury rendering the lung liable to amiodarone's acute toxic damage. These injuries include angiography<sup>19</sup>, cardiothoracic surgery<sup>20</sup>, and lung surgery<sup>21,22</sup> with the most common intraoperative denominator being high inspired oxygen concentrations<sup>23,24</sup>. Patients with preexisting amiodarone lung were found to be at high risk of developing ARDS after cardiothoracic operations<sup>20</sup>. Patients without surgery but ventilated in the ICU have also been found to be at risk of development amiodarone-induced ARDS<sup>25</sup>.

Management of amiodarone-induced ARDS is largely supportive. Steroids have been used empirically. In our patient, given the severe ARDS requiring high concentrations of oxygen to support the patient's oxygenation, empiric use of anti-oxidant therapy was given to minimise further oxygen toxicity. The empiric use of anti-TNF alpha was to combat the likely cytokine storm arising from activation of the alveolar macrophages.

### ***Pharmacotherapy for ARDS***

Research efforts devoted to identifying the magic bullet for combating ARDS have largely been unproductive. In the Cochrane review of 33 randomised clinical trials involving over 3000 patients, no pharmacotherapy was found to show convincing improvement in survival in patients with ARDS. Use of early high-dose steroids in ARDS was deemed not justifiable<sup>26</sup>. The use of corticosteroids in late-phase ARDS remains controversial. An earlier, much quoted, small trial of 24 patients showed improved survival when given moderate dose steroids at day 7 or more after the onset of ARDS, during the so-called fibroproliferative phase of ARDS<sup>27</sup>. A recent multicentre trial of 180 patients however showed higher mortality when given corticosteroids at 14 days or more after the onset of ARDS<sup>28</sup>. Two recent meta-analyses also arrived at conflicting conclusions: the Australian researchers concluded that the use of low-dose corticosteroids was associated with improved mortality and morbidity outcomes<sup>29</sup>, while the U.K. researchers concluded that despite a suggestion of reduced mortality and increased ventilator-free days with steroids after the onset of ARDS, a definitive role of corticosteroids in the treatment of ARDS in adults has not been established<sup>30</sup>. Hence, effective pharmacologic therapy for established ARDS remains controversial and extremely limited.



### Ventilatory Strategy for ARDS

The key advances in the management of ARDS in the past decade lie largely in our better understanding of the mechanisms underlying ventilator-associated lung injury (VALI), which could further exacerbate the ongoing insult to the lung. One important contributor of VALI is regional alveolar overdistension (volutrauma)<sup>31</sup>. Lung-protective strategy using low-tidal volumes at 6 ml per kg of predicted body weight have been proven in the ARDSNET study of over 800 patients to improve ARDS mortality from 40% to 31%<sup>32</sup>. Hypercapnoea is deemed acceptable in this context. Another contributor of VALI is repetitive alveolar collapse with shearing (atelectrauma)<sup>33</sup>. However, despite the interest in the use of high levels of PEEP for addressing the problem of atelectrauma and for alveolar recruitment, the clinical studies of high PEEP levels have not been conclusive<sup>34,35</sup>. Current recommendation on the use of PEEP targets at PEEP levels which can be shown to improve rather than exacerbate the lung mechanics<sup>36</sup>.

### Unconventional Support for ARDS

Two unconventional therapeutic modalities for ARDS have been hotly debated in the past decade: inhaled nitric oxide (iNO) and prone positioning. Both modalities have been aimed to address the key pathophysiological derangement of ARDS: mismatching of ventilation (V) and perfusion (Q) leading to gas exchange impairment. iNO serves as a selective pulmonary vasodilator, offering the theoretical advantage of improving perfusion in areas of better ventilation, thereby enhancing V/Q matching. Over 10 randomised trials on iNO have been conducted in the past decade. Meta-analyses in 2003 and in 2007 both showed no significant effect of iNO on hospital mortality, duration of ventilation or ventilator-free days<sup>37</sup>. There was however improvement in the oxygenation index which persisted till day 4 of therapy. Renal toxicity was noted. Routine use of iNO is not recommended. Some clinicians may still consider iNO as a temporarising measure for life-threatening hypoxaemia.

While iNO may not be readily available in a medical centre, the application of prone positioning can be achieved at the bedside of any ICU. The concept of prone positioning (PP) as a treatment for ARDS arises from the finding of atelectatic lungs in the dependent dorsal regions in a supine patient with ARDS. The reversal from supine to prone positioning allows opening up of the atelectatic lungs, more favourable lung mechanics, better V/Q matching and less VALI<sup>38</sup>. Two recent meta-analyses seemed to have arrived at similar conclusions about the clinical efficacy of PP: PP did not improve survival despite an improvement in oxygenation<sup>39,40</sup>. PP is therefore not recommended as routine treatment for ARDS. However, a sustained improvement in oxygenation may support the use of PP in patients with severe hypoxaemia<sup>40</sup>.

### Conclusion

ARDS represents a severe form of acute lung injury requiring intensive care support. The two cases of fulminant drug-induced ARDS presented here represent triumph in combating a critical condition using conventional as well as unconventional wisdom. As drug-induced ARDS is largely a diagnosis by exclusion, thorough search for other possible aetiologies is a must. Clinicians who regularly use these two drugs, leflunomide and amiodarone, need to keep watchful vigilance on the development of lung toxicity in those patients taking these drugs. Concomittant exposure to other possible pulmonary toxins, such as high-flow oxygen, needs to be avoided as much as possible. Ventilatory support using low tidal volume and optimal PEEP is considered the standard of care. Inhaled nitric oxide and prone positioning are not supported by the literature but nevertheless may serve a temporarising role for those with severe hypoxaemic failure. Pharmacotherapy for ARDS remains very limited.

**Table 1. Clinicopathological entities associated with drug-induced lung disease<sup>4,5</sup>**

Clinicopathologic entity	CT findings	Examples of drugs	Prognosis	Respiratory failure
Hypersensitivity pneumonitis	Bilateral GGO* and poorly defined centrilobular nodules	Methotrexate, gold therapy, cyclophosphamide, nitrofurantoin, antidepressants	Favourable with use of steroids	Yes but infrequently
Eosinophilic pneumonitis	Peripheral alveolar infiltrates	Methotrexate, sulfasalazine, minocycline, para-aminosalicylic acid, nitrofurantoin, NSAIDs	Favourable with use of steroids	Yes but infrequently
Nonspecific interstitial pneumonia	Irregular linear opacities and GGO in subpleural distribution	Amiodarone, chemotherapy	Poor, fibrosis likely	Usually subacute
Desquamative interstitial pneumonia	Bilateral GGO	Methotrexate, interferons, etanercept	Favourable with use of steroids	Yes but infrequently
Diffuse alveolar damage	Diffuse air-space consolidation	Bleomycin, busulphan, mitomycin	Poor; death in 50-60% patients	Yes typically
Non-cardiogenic pulmonary edema	Dependent air-space consolidation	Cytosine arabinoside, beta2 agonists, blood products, narcotics	Favourable	Yes typically
Alveolar hemorrhage	Diffuse air-space consolidation	Oral anticoagulants, fibrinolytic agents, platelet glycoprotein inhibitors	Favourable	Yes typically
Bronchiolitis obliterans organizing pneumonia	Patchy GGO, consolidation and linear opacities	Busulfan, cyclophosphamide, amiodarone, nitrofurantoin, methotrexate	Favourable with use of steroids	Usually subacute

\*GGO = Ground glass opacities

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## MCHK CME Programme Self-assessment Questions

Please read the article entitled "Adult Respiratory Distress Syndrome: Challenges and Triumphs" by Dr. Jane CK CHAN and Dr. Donald YC YU and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 September 2009. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Amiodarone lung disease can be predicted based on the dosage used and the total duration of therapy.
2. Leflunomide-induced lung disease is almost unheard of in the U.K. experience.
3. Amiodarone lung toxicity is exacerbated by its prolonged half life and its lipophilic properties.
4. The clearance of leflunomide can be accelerated by the use of n-acetyl-cysteine.
5. Prior use of methotrexate has been shown to increase the chance of leflunomide-induced lung disease.
6. There have been no significant advances in the management of ARDS in the past 10-20 years.
7. The use of corticosteroids in ARDS is considered standard practice.
8. The use of inhaled nitric oxide has not been proven to improve survival in patients with ARDS.
9. Drug-induced ARDS remains a diagnosis of exclusion, with all efforts required to rule out active infection.
10. Low tidal volume ventilation has been shown to cause ventilator-associated lung injury.



## ANSWER SHEET FOR SEPTEMBER 2009

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2009 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

### Adult Respiratory Distress Syndrome: Challenges and Triumphs

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### Answers to August 2009 Issue

#### Human Swine Influenza

1. T 2. T 3. F 4. F 5. F 6. F 7. T 8. T 9. F 10. F

### Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

Date	Course No	Course Name	Target Participants	CME/CNE
4 Sep 09 - 9 Oct 09 (Every Fri)	C151	Certificate Course on Dental Nursing in Oral Surgery	Dental Nurses	9 CNE Points / CME Accreditation in application
12 Sep 09 - 26 Sep 09 (Every Sat)	C147	Certificate Course on Clinical Ethics in Practice	Professionals in Clinical Practice	6 CNE Points / CME Accreditation in application
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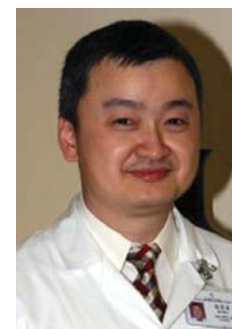
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# Update of Renal Replacement Therapy in the ICU

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## Introduction

In 2004, the term Acute Kidney Injury (AKI) was proposed to represent the entire spectrum of acute renal failure (ARF) with clinical manifestations ranging from a minimal elevation in serum creatinine to anuric renal failure.<sup>1</sup> The reported prevalence of AKI in critically ill patients could be as high as 25% in some developed countries, and only about 4% of this group received renal replacement therapy (RRT), with an ensuing hospital mortality up to 60%. Controversies exist in many aspects of RRT for AKI despite decades of development. However, definitive findings on the dose of RRT were available last year. It is hoped that, with the continued international collaboration, a clearer picture would emerge in other areas of RRT.

## Classification of Acute Kidney Injury The RIFLE Classification<sup>2</sup>

In evaluating the clinical efficacy in AKI studies, meaningful conclusions can only be drawn when there is a common standard of reference. An expert panel from the Acute Dialysis Quality Initiative (ADQI) established a consensus definition called RIFLE in 2002 (www.ADQI.net). In summary, the acronym RIFLE refers to three severity grades (in ascending order of Risk, Injury and Failure) and two clinical outcomes (Loss and End-stage renal failure). The severity grading is based on the change from baseline of either serum creatinine or urine output, whichever is greater. In the subsequent years, RIFLE criteria have been validated by different groups worldwide. With these new criteria, the prevalence of acute kidney injury is 2-to-10 fold greater than previously reported, ranging from 15.4 to 78.3%.<sup>3</sup> RIFLE was also valuable in outcome prediction and correlated well with mortality.<sup>3</sup>

## The AKIN Classification [Table 1]

However, according to the data that have emerged using RIFLE staging criteria, smaller changes in serum creatinine than those considered in the RIFLE criteria might also be associated with adverse outcomes. The ADQI group, and representatives from three nephrology societies (American Society of Nephrology, International Society of Nephrology and National Kidney Foundation) and the European Society of Intensive Care Medicine met and decided to modify the RIFLE criteria. A new classification system, the Acute

Kidney Injury Network (AKIN) Classification, was developed. It retained the emphasis on changes in both urine output and serum creatinine [Table 1]

**Table 1. Acute Kidney Injury Network Classification/ Staging System<sup>a</sup>**

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 26.4 $\mu$ mol/l or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2	Increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours
3 <sup>b</sup>	Increase in serum creatinine to more than 300% (> 3-fold) from baseline (or serum creatinine of more than or equal to 354 $\mu$ mol/l with an acute increase of at least 44 $\mu$ mol/l)	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours

<sup>a</sup> Modified from RIFLE (Risk, Injury, Failure, Loss, and End-stage kidney disease) criteria. The staging system proposed is a highly sensitive interim staging system and is based on recent data indicating that a small change in serum creatinine influences outcome. Only one criterion (creatinine or urine output) has to be fulfilled to qualify for a stage.

<sup>b</sup> Given wide variations in indications and timing of initiation of renal replacement therapy (RRT), individuals who receive RRT are considered to have met the criteria for stage 3 irrespective of the stage they are in at the time of RRT.

## Indications & Timing for RRT

The usual indications for initiating RRT are:

1. Fluid overload unresponsive to diuretic treatment
2. Hyperkalaemia (>6.5 mmol/L or rapidly rising level)
3. Azotaemia (urea >36 mmol/L)
4. Severe acidaemia (pH <7.1)
5. Oliguria (urine output <200ml in 12 hours) or anuria (urine output < 50ml in 12 hours)
6. Uraemia complications like bleeding, pericarditis or encephalopathy

However, in the past decade, the indications for RRT have been extended widely to include many other non-renal indications including:<sup>4</sup>

1. Drug overdose with dialysable or filtratable toxins
2. Patients requiring a large amount of fluid, parenteral nutrient, or blood product but at risk of developing pulmonary oedema or acute respiratory distress syndrome
3. Cardiac failure
4. Hyperthermia or hypothermia (core temperature > 39.5°C or <30°C)
5. Severe dysnatraemia ([Na] >160 mmol/L or < 115 mmol/L)



The concept of 'prophylactic haemodialysis' was first introduced in 1960. Patients with ARF receiving early dialysis tended to have better wound healing, fewer haemorrhages, improved nutritional support and better survival. Since then, blood urea has been regarded as one of the markers for the timing of intervention; the threshold having decreased from 54 mmol/L in the 1960s to 33 mmol/L in 1970s.<sup>5</sup> In the Conger's study of post-traumatic ARF, five out of eight patients survived after receiving early dialysis at a mean blood urea of 18 mmol/L; while only two out of 10 survived when dialysis was initiated at a mean urea of 43 mmol/L.<sup>6</sup>

Survival benefit was also demonstrated in patients suffering from ARF after cardiac surgery. One recent study addressed early versus late intensive initiation of continuous veno-venous haemodiafiltration (CVVHDF) in patients with less than 100 mL urine in the 8 consecutive hours after operation.<sup>7</sup> Early versus late initiation (average lapse 0.88 vs 2.56 days) was associated with reduced ICU stay (8 vs 12 days), reduced ICU mortality (18 vs 48%), and reduced hospital mortality (24 vs 56%).

Nevertheless, this observed benefit could not be repeated in the Bouman's study.<sup>8</sup> One-hundred and six critically ill patients were prospectively evaluated to assess the combined effect of early against late-initiation as well as low-volume (LVHF) against high-volume haemofiltration (HVHF). Patients were randomised into one of the three groups: early HVHF (72-96 L/day), early LVHF (24-36 L/day), and late LVHF (24-36 L/day). On average, the early group started haemofiltration 7 hours after inclusion with the mean starting urea of 17.1 mmol/L; while the late group starting 42 hours after inclusion with a mean urea of 37.4 mmol/L. There was no difference in 28-day mortality nor renal recovery among the three groups.

Thus, the best evidence on the optimal timing for initiating RRT is still lacking and more studies are needed to address these issues. Based on the currently available data and the author's experience, early initiation of RRT is preferable.

## Dose of Renal Replacement Therapy

### Dose Required

While in end-stage renal failure, the delivered spKt/V of 1.2 per dialysis (or urea reduction ratio of 65%) are the accepted minimal standards in reducing morbidity/mortality. The minimum dose for patients with ARF has once been a great controversy in the field of Intensive Care. Thanks to the recent release of two large randomised control trials<sup>9,10</sup> on the dose of RRT for patients with ARF, it has been concluded that there is no evidence to support the use of continuous renal replacement therapy (CRRT) at a dose greater than 25mL/kg/hour. A summary of studies on dosing and outcome in CRRT is listed in [Table 2].<sup>8-13</sup>

The ATN trial (Acute renal failure Trial Network) published in 2008 in the United States did not show any survival benefit with intensive dialysis therapy.<sup>9</sup> This study recruited 1164 critically ill patients with ARF to compare any mortality difference between the

conventional dose group with the more intense dose group. The rate of death was similar; 53.6% in the intensive therapy and 51.5% in the less-intense therapy groups. There was no difference in the duration of RRT or recovery of renal function.

Similarly, the RENAL trial (Randomised Evaluation of Normal against Augmented Level of renal replacement therapy in the ICU)<sup>10</sup> conducted by the Australian and New Zealand group showed no 90-day mortality difference between the conventional dose group and the intensive therapy group (44.68% vs 44.66%,  $p=0.993$ ). This study recruited 1,465 patients with severe ARF in ICUs, who were randomised to receive post-dilutional CVVHDF at 25 mL/kg/h in the conventional group against 40 mL/kg/h in the intensive therapy group. The primary outcome of 90-day mortality showed no difference between the two dosages, and besides, all secondary outcome indicators including ICU mortality, hospital mortality, mechanical ventilation day, ICU length of stay, hospital length of stay, RRT day, RRT dependence at day 28 and day 90 also showed no difference.

## High-volume Haemofiltration (HVHF) in Sepsis Patients

For patients with severe sepsis or septic shock, there is an overwhelming systemic overflow of pro-inflammatory and anti-inflammatory mediators, leading to generalised endothelial damage, multiple organ dysfunction and altered cellular immunological responsiveness. The removal of sepsis pro-inflammatory and anti-inflammatory mediators may help in the treatment of severe sepsis. Cytokines levels in sepsis were found to be lowered only with HVHF (~45ml/kg/h) but not conventional continuous veno-venous haemofiltration (CVVH) (17ml/kg/h).<sup>14</sup> Early animal studies and small scale human trials provided good data on improving the haemodynamic status and survival with HVHF. In the Ronco study published in the Lancet in 2000, although there was no overall survival difference between the two groups with 35 and 45 ml/kg/h doses, a significant survival difference was detected between these groups in a subgroup analysis for patients with sepsis.<sup>11</sup>

A large randomised trial is going on to confirm this unsettled dosing issue in RRT for patients with sepsis. The IVOIRE study (high VOLUME in Intensive care)<sup>15</sup> in Europe will study the use of standard volume (35 mL/kg/h) against HVHF (70 mL/kg/h) in ARF patients with septic shock. It aims to enroll 460 patients to detect a 15% absolute risk reduction in 30-day mortality

## Circuit Patency in CRRT

In an international survey of 345 centres,<sup>16</sup> the major concerns of health care workers about CRRT was the use of anticoagulant, frequent clotting of extracorporeal circuit and the subsequent increased nursing workload. CRRT downtime ranged from 8 to 28% of the total treatment time.<sup>17</sup> Clotting of circuit was the major reason (74%) for the treatment loss. Therefore, it is essential to maintain circuit patency in order to minimise the discrepancy between prescribed and delivered doses.





Commonly used anticoagulants in CRRT are:

1. unfractionated heparin
2. low-molecular-weight heparin (LMWH)
3. citrate
4. prostacyclin / prostaglandin E1
5. nafamostat mesilate
6. direct thrombin inhibitor, e.g. r-hirudin

However, if the use of systemic anticoagulation is contraindicated, one of the alternatives is to flush the system with saline and administer the replacement solution pre-dilutionally. Even with these measures, significant clotting is still encountered in up to 15 to 40% of patients. According to the recently published BEST Kidney multi-national observational study,<sup>18</sup> around one third of the patients received CRRT without any anticoagulation. Among the various anticoagulants, use of un-fractionated heparin ranked the highest (42.9%), followed by regional citrate anticoagulation (9.9%) and then nafamostat mesilate (6.1%)

Unfractionated heparin remains the standard systemic anticoagulant with the benefit of wide clinical experience, low cost, ease of use, ability to monitor the level of anticoagulation and availability of antidotes like protamine if needed. Heparin acts by binding to and activating anti-thrombin III, which in turn inhibits

factors IXa, Xa, and thrombin. The anticoagulant effect can be achieved by giving an initial bolus of 10 to 20 U/kg heparin; followed by continuous infusion of 3 to 20 U/kg/h to achieve 1.5 to 2 times of the normal activated clotting time or activated partial thromboplastin time. For patients at risk of bleeding, a lower dose or a 'tight' heparin regimen with a bolus of 5 to 10 U/kg; followed by infusions of 5 to 10 U/kg/h can be used.<sup>19</sup>

Low-molecular-weight heparin consists of only short polysaccharide chains with average molecular weight in the range of 3000 to 7000 daltons and its biological activity is quantified by the extent of factor Xa inhibition. Hence, dosing differs between different brands of LMWH and the haemofilter used. With respect to unfractionated heparin, LMWH has the advantage of longer half-life, greater bioavailability, dose-independent clearance, less heparin induced thrombocytopenia and less bleeding because of less impact on platelet function. In addition, the half-life of LMWH is prolonged in renal failure and a single injection at start of CRRT usually suffices for up to 5 hours.<sup>19</sup> For example, enoxaparin 40 mg (4000-5000 anti-factor Xa units or 60-70 anti-factor Xa units/kg) can be given as a loading dose, followed by 10 to 40 mg every 6 hours if needed.<sup>19</sup>

TABLE 2. Summary of Studies on Continuous Renal Replacement Treatment (CRRT) Dosing and Outcomes

Study	No.	Randomisations	CRRT mode	Prescribed dose (mL/kg/h)	Delivered dose	Primary outcome	Results
Ronco et al, <sup>11</sup> 2000	425	3 Arms comparing 3 different doses (n=146 vs 139 vs 140)	Post-dilution CVVH: Q <sub>B</sub> 120-240 mL/min	20 vs 35 vs 45	>85% prescribed dose	Survival at 15 days	41% <sup>†</sup> vs 57% vs 58%
Bouman et al, <sup>8</sup> 2002	106	3 Arms comparing EHV vs ELV vs LLV (n=35 vs 35 vs 30)	Post-dilution CVVH: EHV-Q <sub>B</sub> 200 mL/min, Q <sub>R</sub> 72 L/day ELV-Q <sub>B</sub> 100-150 mL/min, Q <sub>R</sub> 24-36 L/day LLV-Q <sub>B</sub> 150 mL/min, Q <sub>R</sub> 24-36L/day	48.2 vs 20.1 vs 19.7	Not mentioned	Survival at 28 days; renal recovery	74.3 % vs 68.8% vs 75% (all except 1 in ELV)
Saudan et al, <sup>12</sup> 2006	206	2 Arms comparing 2 different doses (n=102 vs 104)	Pre-dilution: CVVH (low dose)-Q <sub>B</sub> 100-125 mL/min, Q <sub>R</sub> 1-2.5 L/h CVVHDF (high dose)-Q <sub>B</sub> 100-125 mL/min, Q <sub>R</sub> 1-2.5 L/h, Q <sub>D</sub> 1-1.5 L/h	25 vs 44	Achieved 87 % vs 83% of the delivered dose	28 days survival; 90 days survival	39% <sup>†</sup> vs 59% 34% <sup>†</sup> vs 59%
ATN trial, <sup>9</sup> 2008	1124	2 Arms comparing intense vs less-intense therapy (n=563 vs 561)	CVVHDF: Intensive-Q <sub>B</sub> 150 mL/min, Q <sub>D</sub> 1410 mL/h, Q <sub>R</sub> 1390 L/h Less intensive-Q <sub>B</sub> 140 mL/min, Q <sub>D</sub> 820 mL/h, Q <sub>R</sub> 83 mL/h  For both arms: Haemodynamically unstable-CVVHF/SLED Haemodynamically stable-IHD	36.2 vs 21.5 (for IHD/SLED, 6x/wk vs 3x/wk with Kt/V of 1.2-1.4 per session)	35.8 vs 22.0	60 days mortality	51.2% vs 48.0%
Tolwani et al, <sup>13</sup> 2008	200	2 Arms comparing 2 different doses (n=100 vs 100)	Pre-dilution CVVHDF: Standard dose-Q <sub>B</sub> 100-150 mL/min, Q <sub>D</sub> 1005 mL/h, Q <sub>R</sub> 793 mL/h High dose-Q <sub>B</sub> 100-150 mL/min, Q <sub>D</sub> 1831 mL/h, Q <sub>R</sub> 1406 mL/h	20 vs 35	17 vs 29	Survival to ICU discharge or 30 days	56% vs 49%
RENAL study, By ANZ group <sup>10</sup> 2009	1465	2 Arms comparing 2 different doses (n=743 vs 722)	Post-dilution CVVHDF Q <sub>B</sub> >150 ml/min	25 vs 40	22.0 vs 33.4	90 day mortality	44.68 vs 44.66%

\* CVVH denotes continuous veno-venous haemofiltration; CVVHDF continuous veno-venous haemodiafiltration; EHV early high volume; ELV early low volume; ICU intensive care unit; IHD intermittent haemodialysis; LLV late low volume; Q<sub>B</sub> blood flow; Q<sub>D</sub> dialysate flow; Q<sub>R</sub> replacement rate; SLED sustained low-efficiency dialysis

† Statistically significant

## Regional Citrate Anticoagulation (RCA)

Citrate chelates the calcium in the extracorporeal circuit to mediate its anticoagulant effect.<sup>20-24</sup> This citrate-calcium complex is biologically inert and is partly removed through the haemofilter. The remaining calcium citrate enters the body and mixes with the central venous blood. As the central venous blood flow is much greater than the circuit blood flow rate, the low ionised calcium concentration in the circuit is raised to such a level that any systemic anticoagulant effect is minimal. Therefore, citrate anticoagulation only exists regionally within the circuit. The citrate-calcium complex re-entered the body is dissociated back to free ionised calcium and citrate. All the residual effects of citrate are terminated by the liver, where it is metabolised through the tricarboxylic acid cycle into bicarbonate in a 1:3 ratio. To prevent filter clotting, a pre-filter citrate concentration of 3.5 to 4 mmol/L is needed to keep the ionised calcium concentration in the circuit to below 0.25 mmol/L.<sup>19,21</sup> Because of the net loss of calcium in the form of citrate-calcium complex in the ultrafiltrate, a small amount of calcium supplement is needed. It is usually given intravenously via a separate central venous line and its rate is titrated to give a normal ionised calcium concentration.

Citrate is commonly formulated in 4% tri-sodium citrate or anticoagulant-citrate-dextrose A (ACDA) or as proprietary products like Gambro Prismocitrate 10/2 and Fresenius multiFiltrate Ci-Ca system (4% tri-sodium citrate).

The advantages of using RCA are:<sup>25-28</sup>

1. longer circuit / filter life
2. safe for use even in patients with bleeding tendency or who had recent surgery
3. less microthrombi formation within filter tubules
4. less platelet activation
5. less blood transfusion required

Although RCA is superior in keeping circuit patency, the metabolic problems associated with it make it unpopular. These include: hypernatraemia, metabolic alkalosis and the potential for hypocalcaemia (secondary to accumulation of citrate). The contraindications for RCA are severe liver dysfunction and massive blood transfusion. Its underlying rationale is the increased risk of citrate accumulation causing toxicity. Citrate toxicity should be suspected whenever ionised calcium is persistently low or the total to ionised calcium ratio is higher than 2.5.<sup>22</sup> Symptoms of hypocalcaemia include paraesthesia, nausea, cramps, tetany, hypotension, decrease in cardiac output, or a prolonged QT interval.<sup>19</sup>

In order to reduce the metabolic side effects related to RCA, the concentrations of sodium and bicarbonate in the replacement solution, during RCA setup, should be carefully adjusted. Close monitoring of electrolytes including sodium, potassium, arterial blood gases, ionised and total calcium, during CRRT, is essential.

RCA has been adopted as the default mode for CRRT in our department since 1995. Our experience with RCA is promising. It is safe and well accepted by our doctors and nurses. Overt metabolic complications have never occurred.

## Conclusion

AKI is common among the critically-ill and RRT is frequently used to support these patients. Emerging international consensus classification is available to better stratify AKI patients so that future studies are meaningful for comparison. Although the adequacy of RRT dosing has been determined in recent good quality trials, there still exist areas of uncertainties about RRT. Further studies are needed to address the indications, optimal timing of initiation and the types of anticoagulants.

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## Molecular Adsorbents Recirculating System (MARS): Evidence and Management Pitfalls

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Liver failure, regardless of aetiology, is a disease of excessive mortality, and the only effective treatment so far is liver transplantation. Because of organ shortage, patient instability and various other reasons, liver transplantation may not be performed in time in many occasions. Throughout time, different artificial liver support systems have been developed with the hope of filling this time gap by temporarily supporting the liver and stabilising the patient so that one can be bridged to transplantation.

Molecular Adsorbents Recirculating System (MARS) is a non-biological artificial liver support system developed according to the prototype designed by Stange and Mitzner at the University of Rostock, Germany, in 1993<sup>1</sup>. MARS is a form of blood purification system that utilises albumin as dialysate to remove protein-bounded toxins in patients of liver failure<sup>2</sup>. The system consists of three interconnected circuits. The patient's blood cycling in an extracorporeal circuit is dialysed against an albumin circuit through a specific dialyser running in countercurrent. The membrane of the dialyser is impermeable to albumin molecules, essential proteins or hormones, but it allows the transport of bilirubin and other toxins across it by means of a non-energy-dependent process known as ligandification and deligandification into the albumin dialysate circuit. The dialysate is then regenerated online after passing through a charcoal adsorption column and an anion exchange resin column. Hydro-soluble toxins, urea, excessive electrolytes and fluid are regulated through a third circuit, which can be a standard haemodialysis machine or a continuous renal replacement therapy (Figure 1).

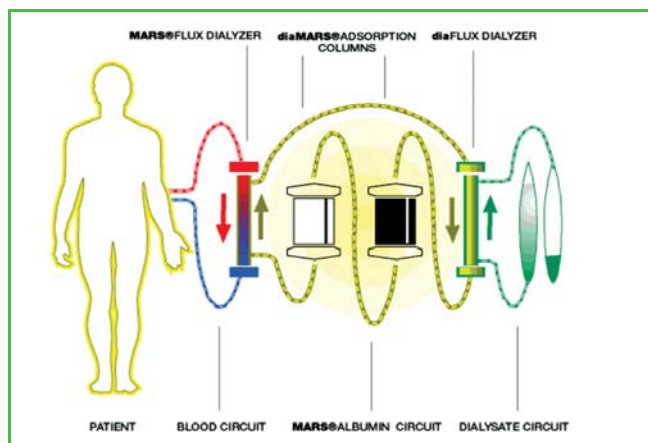


Figure 1 :The MARS circuit (with permission from Gambro, Inc)

### Evidence

Evidence relating to the efficacy of MARS can be categorised into three levels: biochemical efficacy, physiological improvement, and clinical benefits. The biochemical efficacy of MARS has been well proven. Toxins as removable by MARS documented in the literature include bilirubin, ammonia, aromatic amino acids, tryptophans, short-chain fatty acids, bile acids, GABA-like substances, nitric oxides and cytokines<sup>3</sup>. Most of the toxins removable by MARS are implicated in the development of hepatic encephalopathy, portal hypertension or other inflammatory changes in liver failure. Amongst all, reduction of bilirubin, either total or direct, is the most consistent as demonstrated by all studies. It should be noted that bilirubin, at least in adult patients, is not a deadly toxin as such. Its use is mainly regarded as a surrogate marker for other hepatotoxins that are not routinely measured in daily clinical practice.

The physiological benefits demonstrated by the MARS system include lowering of intracranial pressure (ICP), reduction of portal pressure, and improvement of blood pressure and systemic vascular resistance. Reduction of ICP in liver failure by MARS was first reported in animal studies<sup>4</sup> and subsequently also in a case report<sup>5</sup>. Elevated ICP implies cerebral oedema which is one of the most common causes of death in patients with acute liver failure. Reduction of ICP implies that cerebral oedema is under control and the patient may be able to gain more time to bridge to transplantation.

In patients with liver failure, particularly those with cirrhosis, portal hypertension is a significant factor contributing to ascites formation, variceal bleeding and hepatorenal syndrome. MARS has been shown to be able to reduce the hepatic venous pressure gradient, an indirect measurement of portal pressure. This effect is not only observed during treatment, but sustained for up to 24 hours after MARS<sup>6</sup>. The mechanism of reduction of portal pressure is unknown, but is believed to be mediated through removal of vasoactive substances like nitric oxide in the splanchnic circulation by MARS.

The haemodynamic benefits brought about by MARS in patients having liver failure include raised mean arterial pressure, increased systemic vascular resistance, and reduced cardiac output. Haemodynamic effect is particularly prominent in patients with cirrhosis during treatment<sup>7,8</sup>. In patients with acute liver failure,



increased vascular tone could also be observed, but the result is not as sustained<sup>9</sup>. These findings illustrate that MARS is haemodynamically well tolerated and would not cause hypotension as such. From our experience, however, we find transitory hypotension rather common at the beginning of treatment, and small doses of vasopressor are frequently needed to sustain blood pressure. We attribute this to release of cytokines secondary to platelet activation and change in rheology of blood<sup>10</sup> circulating through the extracorporeal system.

The effects of MARS on two most common complications of liver failure have been studied. Mitzner et al. reported a significantly lower mortality rate in patients with type 1 hepatorenal syndrome treated with MARS compared with those having standard medical therapy<sup>11</sup>. The major shortcoming of this study was that there were only 13 patients involved and in fact only one patient in the treatment survived beyond 30 days. Earlier studies of MARS on hepatic encephalopathy were mainly non-randomised studies and reported lower mortality in treatment groups<sup>12</sup>. Hassanein et al. reported the use of MARS in patients with severe hepatic encephalopathy in a large-scale randomised controlled trial and concluded that the treatment was associated with earlier and more frequent improvement in encephalopathy grading<sup>13</sup>. It should be noted, however, that the trial was not designed to address the impact of MARS on survival.

MARS is not without complications. The most common complication of MARS is platelet reduction. In our experience, the drop in platelet per treatment is around 5 to 10%, but it may be up to 20% in some cases. Though it might not seem significant in most patients with platelet count more than  $100 \times 10^9/L$ , it does raise concern in cirrhotic patients with splenomegaly in which they commonly have thrombocytopenia to start with and when repeated treatments are needed. We empirically give platelet transfusion before MARS to patients with platelet count less than  $30 \times 10^9/L$ . In our experience, four major bleeding episodes might have been related to MARS (2 intracranial bleeding, 1 variceal bleeding and 1 intra-abdominal bleeding after liver transplantation). However, given the inclination of developing these complications in such critical patients, it may be unjustifiable to attribute occurrences of these episodes to MARS. Worldwide, the opinion is that MARS treatment is safe and does not cause additional bleeding risk.

Other documented complications of MARS include hypoglycaemia during treatment<sup>14</sup>, electrolyte disturbances<sup>15</sup>, and non-cardiogenic pulmonary oedema<sup>16</sup>. As MARS is one form of extracorporeal circuit, it shares the potential complications that extracorporeal circuits usually have, including catheter-related infection, haematoma and circuit thrombosis.

Anticoagulation in treatment by MARS is a difficult topic. In our unit, we have moved from no anticoagulation to the use of low molecular weight heparin, and then to heparin priming in which the system is flushed with heparin saline before use. Given the nature of the disease of patients treated, we have not used systemic anticoagulation, albeit it is claimed to

be safe according to other centres' experience. The coagulation profile of patients with liver failure varies significantly and represents the interplay between thrombocytopenia, platelet dysfunction and also reduced synthesis of clotting factors and antithrombin from liver. In order to develop a tailor-made anticoagulation strategy, some researchers have advocated the use of thromboelastography (TEG) to monitor these patients during treatment<sup>17,18</sup>. We have also tried to apply this monitor in our practice, but because TEG interpretation is in itself open to a lot of debate, we feel that it is still a research tool rather than for routine clinical use. Circuit thrombosis is not necessarily due to inadequate anticoagulation. Circuit blood flow and turbulences, as well as position and properties of the dialysis catheter, could be contributing factors to inadequate anticoagulation.

## Management Pitfalls

MARS is by no means a salvage treatment for liver failure. The most serious management pitfall is implementing MARS as a last resort hoping that the treatment can reverse the detrimental effects of liver failure at a time when the patient is already moribund. In our practice, we employ MARS as an early intervention to prevent deterioration, preferably when the patient is not too ill. We render MARS treatment to those showing rapid velocity but not high absolute value in biochemical deterioration, those with grade 2 hepatic encephalopathy, and those with hepatorenal syndrome with urine output still more than 0.5ml/kg/hr. We believe it is at these time points that MARS can alleviate organ damage and retard progression of the disease through hepatotoxin removal. On the contrary, if MARS treatment is rendered late in the course of liver failure, the benefit of hepatotoxin removal will become minimal amidst the overwhelming cascade of physiological damages brought about by multi-organ failure<sup>19</sup>.

Another management pitfall is indiscriminate use of MARS for all patients with liver failure. In fact, MARS is not applicable to all patients; only a selected few can benefit from it. The selection criteria for MARS candidates in our unit are listed in Table 1. Based on these criteria, less than 25% of the patients admitted with liver failure to our intensive care unit are eligible for the treatment. Certain subgroups of patients, such as those with acute decompensated Wilson disease, have appeared to respond particularly well to MARS<sup>20</sup>. Selection of suitable candidates and initiation of MARS at appropriate timing are the two most important factors to improve the success rate of MARS treatment.

The third management pitfall is utilising MARS as a means to reverse liver failure. Although native liver recovery with MARS has been reported in the literature and also occasionally encountered in our experience, it is unpredictable as to which patients will respond favourably. It is therefore inappropriate to commend the treatment as one which can promote liver recovery. In our centre, the sole objective of performing MARS is to stabilise patients' conditions and to bridge them to transplantation. It should be clearly explained to patients who are undergoing MARS but not aiming for liver transplantation that the treatment would only



bring about short-term improvement to their conditions. Hopefully, recognition and appropriate future consideration of these management pitfalls will offer possibilities for further refinement of the use of MARS in patients with liver failure.

## Conclusion

Since MARS was first launched into clinical application in year 2000, research materials published on this topic have exceeded 500, mostly descriptive studies with only a handful of randomised trials amongst them. Given the lack of concrete evidence to demonstrate the survival benefit of MARS, it is understandable that clinicians are skeptical to commit to such treatment which is expensive to run, has a complex operative procedure, and, most importantly, not without risk. It should be noted, however, that liver failure is a disease associated with high mortality and limited treatment options. Any suggestion or evidence, despite being observational or uncontrolled, should therefore not be overlooked and neglected casually. Moreover, the lack of conclusive result from randomised controlled trials could also be due to fallacies and limitations of study methodology. Heterogeneity of the disease, existence of confounding factors, e.g. availability of liver transplantation, and lack of reliable tools to prognosticate patients and to monitor treatment efficacy are all factors that need to be considered in the design of studies on MARS.

In summary, utilisation of MARS treatment requires a comprehensive understanding of its benefits and limitations if optimal outcome is to be achieved. Further studies to delineate and refine the clinical indications, timing of initiation and operative details are needed to give clinicians a better idea of how to implement such service in practice.

## Competing Interests:

Nothing to declare.

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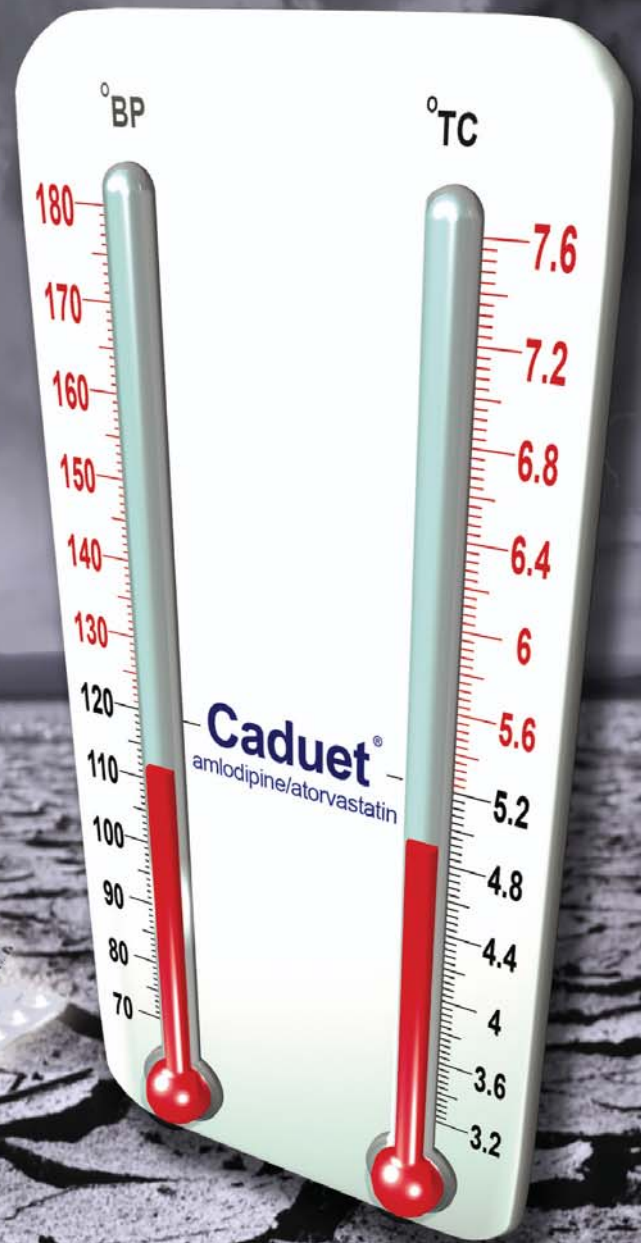
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## Mechanical Circulatory Support in the Intensive Care Unit

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Acute circulatory failure resulting in cardiogenic shock is a common problem encountered in the intensive care unit. Cardiogenic shock is defined by the presence of the following haemodynamic parameters: sustained hypotension (systolic blood pressure <90mmHg or mean arterial pressure of 30mmHg below basal level), adequate or elevated left ventricular (LV) filling pressure (e.g. left ventricular end-diastolic pressure >18mmHg or right ventricular end-diastolic pressure or pulmonary artery wedge pressure > 15mmHg) and reduced cardiac output (cardiac index <1.8L/min/m<sup>2</sup> without support or <2.0-2.2 L/min/m<sup>2</sup> with support). Clinical manifestations of cardiogenic shock include signs of poor tissue perfusion such as cold extremities, oliguria and/or clouded sensorium, in the setting of myocardial dysfunction. Causes of cardiogenic shock include acute myocardial infarction with or without mechanical complications (e.g. ventricular septal rupture, papillary muscle rupture with acute mitral regurgitation, contained free wall rupture), acute myocarditis, takotsubo (or stress-induced) cardiomyopathy, acute valvular regurgitation, or any other cause of acute severe left ventricular (LV) or right ventricular (RV) dysfunction.

The mainstay of treatment for cardiogenic shock is pharmacological support using inotropic agents, such as dobutamine, dopamine and norepinephrine, and phosphodiesterase inhibitors, such as milrinone. These agents improve short-term haemodynamics at the expense of increased oxygen demand by increasing myocardial ATP consumption, which may be deleterious over long-term. Calcium-sensitising agents with inodilatory properties such as levosimendan, which does not increase oxygen demand and is less pro-arrhythmic, have been shown to have a statistically non-significant but consistently lower mortality than dobutamine at six months in the treatment of acute decompensated heart failure<sup>1</sup>. Another agent which may be used to treat acute decompensated heart failure is a recombinant B-type natriuretic peptide called nesiritide. However, pooled analysis of randomised controlled trials showed increased risk of death at 1 month<sup>2</sup> and worsening renal function with nesiritide compared to usual therapy<sup>3</sup>.

## Mechanical Circulatory Support

In circumstances where a potentially reversible cause of acute heart failure has been identified or where cardiac surgery or transplantation is considered an option for refractory heart failure, mechanical circulatory support systems are available which can maintain the patient until definitive treatment is instituted. Mechanical circulatory

support can be life-saving in acute cardiogenic shock and particularly useful as a bridge to recovery in cases of fulminant myocarditis. There is evidence that patients with fulminant myocarditis, i.e. those with severe haemodynamic compromise, rapid onset of symptoms and fever, have a better long-term prognosis than those with acute nonfulminant myocarditis if they survive the initial period of cardiogenic shock<sup>4</sup>. Therefore, in these patients, an aggressive approach including mechanical circulatory support is warranted. Time from onset of illness to recovery of ventricular function in fulminant myocarditis usually takes 2 to 3 weeks<sup>5</sup>. Mechanical circulatory support includes placement of intra-aortic counterpulsation balloon pumps (IABP), extracorporeal membrane oxygenation systems (ECMO), and ventricular assist devices (VAD).

## Intra-aortic Balloon Pump (IABP) or Counterpulsation

Intra-aortic balloon pump (IABP) is the most commonly used mechanical support for cardiogenic shock. The IABP is commonly inserted percutaneously through the femoral artery (Figure 1) but, in patients with peripheral vascular disease, it may be inserted through the brachial artery<sup>6</sup>. By synchronising inflation and deflation to the patient's cardiac cycle, the IABP improves coronary and peripheral perfusion during diastolic balloon inflation and augments left ventricular performance during systolic balloon deflation by reducing the afterload (Figure 2).

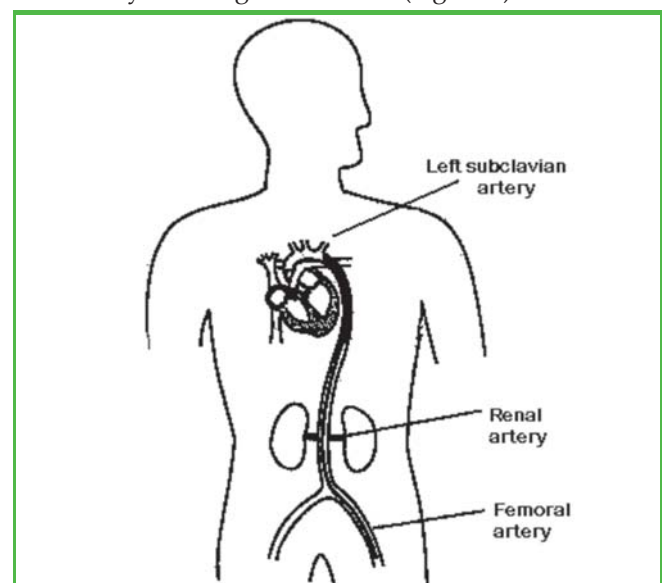


Figure 1. The IABP is inserted percutaneously via the femoral artery and positioned in the thoracic aorta distal to the left subclavian artery and proximal to the renal arteries

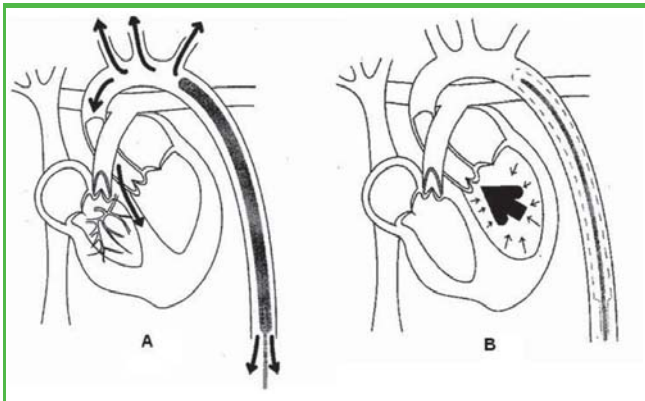


Figure 2. Inflation and deflation of the IABP are synchronized to the patient's cardiac cycle - A. With balloon inflation during diastole, there is increased coronary artery blood and systemic perfusion; B. With balloon deflation during systole, oxygen demand is reduced, resulting in increased stroke volume and reduced afterload.

Apart from left ventricular failure and cardiogenic shock, indications for IABP include support of high risk patients for percutaneous coronary intervention, cardiac surgery for post-myocardial infarction ventricular septal defect or acute mitral regurgitation, stabilisation of heart failure patients undergoing general anaesthesia and bridge to heart transplant. Its use is contraindicated in severe aortic valvular insufficiency which may worsen during diastolic regurgitation, aortic dissection, peripheral vascular disease and tachyarrhythmias.

Vascular complications associated with the use of IABP include limb ischaemia, aortic or arterial injury such as perforation and dissection, femoral artery thrombosis, peripheral embolisation, and visceral ischaemia. Other complications may be balloon related (such as incorrect positioning, gas embolisation) or related to infection or entrapment. In patients with peripheral vascular disease and diabetes, sheathless method rather than sheathed technique should be used<sup>7</sup>.

## Extra-corporeal Membrane Oxygenation (ECMO)

ECMO is a form of extracorporeal life support whereby an external pump system carries the venous blood from the large central veins of the patient to an oxygenator (a gas exchange device) where the blood becomes enriched with oxygen and has carbon dioxide removed. The oxygenated blood then re-enters the patient's circulation, either through the aorta or arterial system (so-called veno-arterial ECMO) (Figure 3) or through the venous system (veno-venous ECMO). Veno-arterial ECMO provides support for severe cardiac failure with or without respiratory failure and can be set up by using peripheral cannulation of the femoral artery and vein (Figure 4), so-called percutaneous cardiopulmonary support system (PCPS). Veno-arterial ECMO may be applied for the short-term management of cardio-respiratory failure or cardiac failure refractory to inotropic and IABP support. Common indications include acute fulminant myocarditis<sup>8</sup>, severe acute respiratory distress syndrome (ARDS)<sup>9</sup>, acute decompensated dilated cardiomyopathy, ischaemic cardiogenic shock, drug overdose or sepsis with profound cardiac depression and as a bridge to longer-term ventricular assist device<sup>10</sup>. Veno-venous ECMO

involves return of oxygenated blood to the venous system of the patient, usually the right atrium via the internal jugular vein, and is the preferred mode of support for isolated respiratory failure, such as ARDS<sup>11</sup>. In ARDS, ECMO provides life support without reliance on high-pressure high-oxygen mechanical ventilation for gas exchange, thereby reducing the release of inflammatory mediators from the damaged native lung, and buys time necessary for the lung to heal.

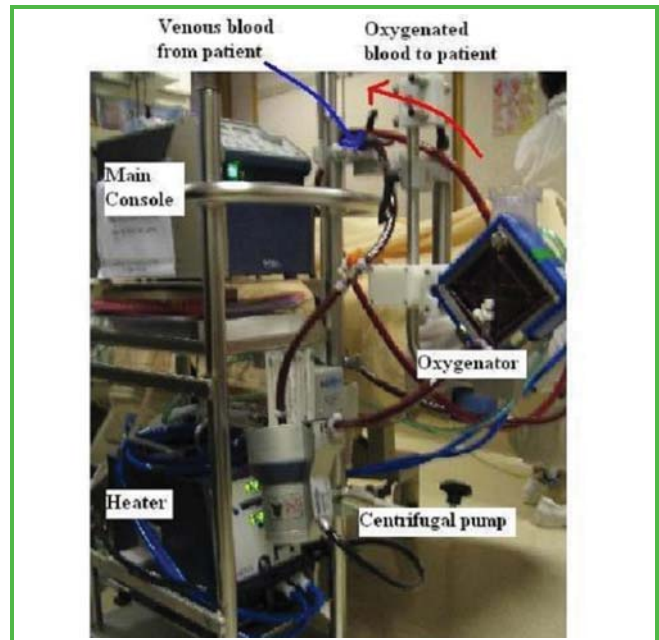


Figure 3. Different components of an ECMO system - the main console controls the flow rate of the centrifugal blood pump, which drives the venous blood from the patient through the oxygenator prior to returning the blood to the arterial side of the patient's circulation.

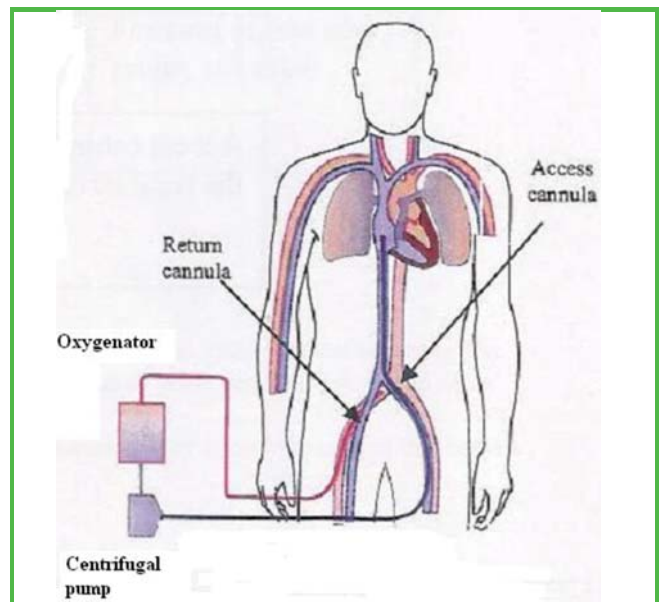


Figure 4. Blood is accessed from the large central veins such as the inferior vena cava and returned to the arterial system in the aorta after passing through the oxygenator of the ECMO system.

The major components of ECMO involve the blood pump ('the heart') and the oxygenator ('the lung'). Previously roller pumps were standard for ECMO therapy but the mechanical stress results in rupture and embolism of tube particles. These complications are avoided with the use of centrifugal pumps. The



duration of ECMO support depends on the type of oxygenator used. With silicone-membrane or microporous hollow-fibre oxygenators, plasma leakage typically occurs after a few days, necessitating circuit changeover. However, with diffusion membrane oxygenators such as the QuadroxD (Jostra Medizintechnik AG, Hirrlingen, Germany), the hollow-fibre technology utilises a true non-microporous membrane and avoids plasma leak problem. The system is ideal for prolonged perfusion up to 14 days with the longest duration reported to be 46 days<sup>12</sup>.

Like the IABP, the PCPS is also contraindicated in aortic dissection and severe aortic valve regurgitation. Potential complications associated with the use of ECMO include vascular complications, haemolysis, mechanical problems with clots or air in the system, oxygenator thrombosis and bleeding tendency with use of heparin.

In case of IABP failing to support the patient, PCPS or V-A ECMO can immediately provide adequate perfusion to all organs irrespective of the lung condition. However, PCPS cannot augment coronary blood flow and may increase left ventricular afterload. Combination of IABP and PCPS is clinically feasible and has been shown in animal models to have important advantages over PCPS alone, especially in ischaemic cardiomyopathy<sup>13,14</sup>. Combined use of IABP and ECMO reduces left ventricular wall stress and oxygen consumption while increasing the end-systolic elastance<sup>13</sup> and reduces tissue acidosis and myocardial necrosis<sup>14</sup>.

## Ventricular Assist Devices (VAD)

Patients with advanced heart failure in New York Heart Association class III and IV may be classified into seven clinical profiles in the Interagency Registry of Mechanically Assisted Circulatory Support (INTERMACS) to allow optimal selection for mechanical circulatory support, especially ventricular assist devices (VAD). 80% of such devices are being used in the two profiles with the highest levels of clinical compromise, namely those "crash and burn" patients (INTERMACS profile 1) and "sliding on inotropes" patients (INTERMACS profile 2)<sup>15</sup>. There are many types of VAD, with the first-generation VAD being pulsatile devices, the second-generation VAD being the axial flow pumps and the third-generation VAD being centrifugal pumps which are bearingless and designed for long-term support. In the past, use of the extracorporeal or implantable VAD requires surgical implantation in the operating theatre. Recently, VAD which may be inserted percutaneously have been developed for clinical use. For example, the TandemHeart Percutaneous Ventricular Assist Device (pVAD) is an extracorporeal continuous-flow centrifugal pump. A cannula is inserted through the femoral vein, across the interatrial septum and into the left atrium. The TandemHeart pump withdraws oxygenated blood from the left atrium and returns it to one or both femoral arteries via arterial cannulas (Figure 5). Compared with IABP, the pVAD can provide better haemodynamic improvement, in terms of increased cardiac output, reduced pulmonary wedge

pressure and higher mean arterial pressure<sup>16,17</sup>, and lower serum lactate level<sup>17</sup>. Potential complications with this device include limb ischaemia, disseminated intravascular coagulation (DIC), bleeding from cannulation site and infection. Another device called the Impella Recover LP 2.5 is a minimally invasive catheter-based ventricular assist device, which is inserted using the Seldinger technique through the femoral artery. The tip of the catheter contains a "pigtail" which rests in the left ventricle<sup>18</sup>.

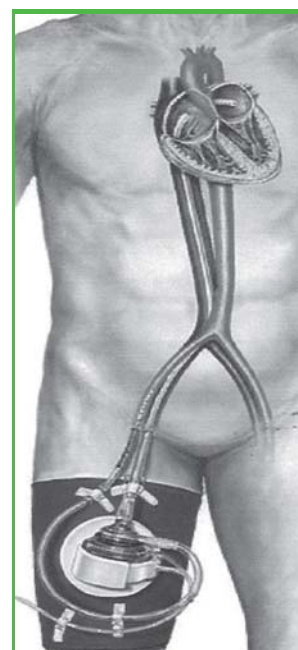


Figure 5. Diagrammatic representation of a percutaneous ventricular assist device (pVAD) which withdraws oxygenated blood from the left atrium and returns it to the femoral artery via arterial cannula

## Evolving Role of Mechanical Circulatory Support

Nowadays, VAD is not only used as a bridge to heart transplantation in severe heart failure but increasingly used as a bridge to myocardial recovery or as destination therapy (i.e. for permanent use in patients who are not candidates for heart transplantation). There is evidence that, in some severe heart failure patients, prolonged complete unloading of the left ventricle (LV) with VAD may lead to structural reverse remodelling and functional improvement of the LV. This is true not only in myocarditis patients<sup>19</sup> but also in non-ischaemic dilated cardiomyopathy patients<sup>20</sup>. The time frame for myocardial recovery can vary from weeks to months. Currently the use of implantable long-term VAD is associated with major complications such as embolic stroke, mechanical device failure, infection and need for sternotomy. Development of bearingless centrifugal pumps, smaller devices and partial cardiac support system which can be implanted with a minimally invasive procedure<sup>21</sup> will hopefully minimise some of the problems.

## Conclusion

At present, IABP, ECMO and VAD are available as mechanical circulatory support for cardiogenic shock. The IABP is convenient to be applied but can only provide limited additional cardiac output, which may not be adequate for critical situations. ECMO can provide total circulatory support but suffers the drawback of extracorporeal circulation such as activation of cellular elements and the need of an oxygenator. The duration of use is limited to 2 to 6 weeks. Implantable VAD has the potential to provide



weeks. Implantable VAD has the potential to provide longer-term support but the device is expensive and implantation requires surgical expertise. Percutaneous VAD and partial mechanical cardiac support, currently under investigation, are attractive alternatives because of ease of insertion but are not yet widely available.

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# Infectious Disease Emergencies

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Infectious disease emergencies (IDEs) are not uncommon. However, even in a classical infectious diseases textbook, only intracranial infection, bacteraemia, and fulminant pneumonia are included in the relevant chapter. In practice the spectrum of IDEs manifesting in an inpatient setting is much wider<sup>1,2</sup>. We define or will define as any clinically and microbiologically documented infection that by itself or as a complication of its treatment is liable to result in (i) irreversible local tissue or organ damage, permanent functional loss, or (ii) imminent death without urgent medical or surgical intervention or progressive system inflammatory response syndrome, to the extent that advanced life support or intensive care would soon be required.

## Strategies in the Diagnosis of IDE

Constant vigilance, a systematic approach to any clinical problem, and timely consultation will enable early detection of conditions requiring urgent treatment, so that optimal management may be implemented early to prevent irreversible complications or death. All infections may initially be minor and appear innocuous, such as cellulitis developing from an inapparent skin wound. However, if the initial infective process is uncontrolled by the host defence mechanisms or appropriate therapy, it may result in potentially life-threatening diseases, such as group A streptococcal necrotising fasciitis or *Streptococcus suis* meningitis. It is essential that the diagnosis be made when the area of necrosis or extent of meningeal involvement is still limited. At this early stage, even though the pathology has been established and bacteria could be isolated from tissues or CSF, the clinical signs may not be typical. Nevertheless, the benefit of correct treatment at this stage is the greatest. Similarly, antibiotic-induced morbilliform rash is not an IDE, but erythema multiforme involving the mucosa heralds one. It may be too late if an IDE is declared only when frank skin exfoliation or gastrointestinal bleeding occurs. The clinical examples of IDEs encountered in our clinical consultation service are listed in Table 1.

## Causes for Failure to Make an Early Diagnosis

Failure to recognise an emergency was related to several factors, the commonest being a presentation that does not conform to classic descriptions of the disease, such as deafness rather than neck rigidity in acute pyogenic meningitis. Furthermore, typical features may present in an atypical clinical setting. For example, CMV retinitis is a well-known complication in HIV-infected

patients, requiring urgent anti-viral treatment, but suspicion of this entity may not be raised in non-AIDS cases. This illustrates the need to account for each acute clinical manifestation despite apparent incongruence.

Sometimes, diseases usually not directly related to the clinical specialty of the referring clinicians may also be missed. In this era of specialisation, clinicians often rely on their colleagues to deal with problems that do not fall strictly within their specialty. Thus, a considerable number of adverse reactions to antimicrobial agents were not recognised early.

Clinicians may also face difficulties with uncommon organisms and their associated pathology such as *Bartonella henselae*, rickettsiae, *Leptospira*, *Haemophilus aphrophilus*, and *Vibrio vulnificus*. Similarly, rare complications of common infections may not be appreciated such as *Clostridium difficile*-related toxic megacolon. A better liaison between the infectious disease specialist and the clinician can enable mutual exchange of knowledge and experience and ultimately result in improved care of patients in the early stages of an IDE.

Table 1. Examples of infectious disease emergencies encountered in the clinical consultation service at the Department of Microbiology, Queen Mary Hospital.

Organ system	Examples
Central nervous system and eye	<ul style="list-style-type: none"> <li>Acute meningitis</li> <li>Cerebral and epidural abscess</li> <li>Cytomegalovirus retinitis</li> <li>Subdural empyema, endophthalmitis, cavernous sinus thrombosis, VZV anterior uveitis and keratitis, rhinocerebral mucormycosis</li> </ul>
Cardiovascular system	<ul style="list-style-type: none"> <li>Infective endocarditis</li> <li>Infected aortic aneurysm or graft</li> <li>Pyopericardium, cardiac tamponade</li> </ul>
Upper respiratory tract	<ul style="list-style-type: none"> <li>Imminent upper airway obstruction, e.g. mucositis, abscess</li> <li>Fungal sinusitis, rhinocerebral mycosis</li> </ul>
Lower respiratory tract and thorax	<ul style="list-style-type: none"> <li>Fulminant pneumonia</li> <li>Miliary tuberculosis</li> <li>Cavitary pneumonia with pneumothorax</li> <li>Massive haemoptysis (aspergillosis in old tuberculous cavity)</li> <li>Procedure-related mediastinitis</li> </ul>
Alimentary system and peritoneum	<ul style="list-style-type: none"> <li>Tertiary peritonitis</li> <li>Toxic megacolon (amoebic, typhoid)</li> <li>Neutropenic ileocaecitis</li> <li>Emphysematous cholecystitis</li> </ul>
Skin and soft tissue	<ul style="list-style-type: none"> <li>Necrotising fasciitis and Fournier's gangrene</li> <li>Gas gangrene</li> <li>Orbital cellulitis</li> </ul>
Bone and joint	<ul style="list-style-type: none"> <li>Pyogenic arthritis</li> </ul>
Systemic	<ul style="list-style-type: none"> <li>Sepsis in immunocompromised patients including post-splenectomy sepsis and neutropenic sepsis</li> <li>Severe sepsis and others*</li> </ul>
Antibiotic-induced	<ul style="list-style-type: none"> <li>Hepatitis, renal failure</li> <li>Xanthopsia, hearing loss</li> <li>Allergic reactions</li> <li>Convulsion</li> </ul>

\*Including gas gangrene, tetanus, severe falciparum malaria, hantavirus haemorrhagic fever with renal syndrome, chickenpox in an oncology patient, dengue haemorrhagic fever, bleeding due to severe thrombocytopenia as a result of rubella and infectious mononucleosis, toxic shock syndrome, perinephric abscess, emphysematous pyelonephritis, pyonephrosis.



## Management of IDE

Regarding the care of patients with IDEs, the commonest contribution of the infectious disease specialist is to advise on the choice of appropriate antimicrobials. The proficiency of infectious disease specialists in antimicrobial chemotherapeutics also enables them to initiate modification of the dosage or route of administration as appropriate. Another contribution of the infectious disease team is the delineation, after thorough evaluation of patients and further investigations, of problems that were not apparent to the referring clinician. For example, necrotising fasciitis due to *V. vulnificus* is known to be rapidly progressive, and an early diagnosis can make a significant difference in the eventual outcome. Our experience is that needle aspiration is pivotal in establishing an aetiological diagnosis and indicating the choice of antimicrobials. Early extensive debridement, as guided by the Gram smear of the resection margin, is crucial for a favourable outcome. In the long run, the infectious disease team will help to raise the awareness of this IDE, alerting clinicians to future occurrences of similar conditions, and recognising the early outbreak of deadly disease like SARS<sup>3</sup>.

## Clues to Early Recognition of IDE

Patients with a systemic inflammatory response should be carefully evaluated for any underlying focus of infection that may not be apparent initially. Occupational history, local signs, or subtle radiological findings can also be useful pointers to the diagnosis and its emergency nature. Any condition involving vital organs such as the central nervous system (brain, spinal cord, and eye), the cardiovascular system (especially heart valves), and the upper airway should alert clinicians to the potential for irreversible damage due to an infection. Emergencies can arise as a result of serious toxicity from treatment; they are usually due to drugs, including hypersensitivity reactions, potentially irreversible organ toxicity, or other side effects.

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# Sedation and Analgesia in the Intensive Care Unit

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## Introduction

Critically ill patients in the intensive care unit (ICU) requiring mechanical ventilation frequently experience pain, anxiety, sleep deprivation and distress. Sedation and analgesics are commonly used to provide comfort and relieve pain. Commonly used agents include benzodiazepines, propofol, opioids and the newer agents, remifentanyl and dexmedetomidine.

There is now an increasing awareness that important complications from sedative agents and the way they are used, can occur.<sup>1</sup> Oversedation can prolong weaning from ventilation and ICU duration of stay.<sup>2</sup> Undersedation may contribute to increased sympathetic activity, myocardial ischaemia, poor ventilator synchrony, hypercatabolism, immunosuppression and accidental dislodgements of lines and tubes. Finally, sedation and analgesia may increase delirium, which can occur in up to 80% of ICU patients, without achieving increased comfort.

Current practice varies widely.<sup>1,3</sup> New trends and research are therefore focused not only on which is the best pharmacological agent, but also on monitoring the depth and adequacy of sedation and protocols sedation use.

## Indications for Sedation

Appropriate evaluation and management of causes of distress are essential to optimal management of sedation. Preexisting medical conditions such as alcohol or substance abuse, chronic sedative use, psychiatric illness, alzheimers, gout, chronic pain may contribute to the experience of distress and influence choice of agent.<sup>4</sup> Identifying new causes of pain related to the acute illness is also crucial. Management of root causes such as bedsores, wound infections and changing medical conditions should not be masked by use of sedatives. Simple measures such as frequent turning, removing restraints if possible, or minimizing light and noise to allow night time sleep patterns may also improve patient comfort. Communication and explanation to the patient during interventions can significantly allay anxiety.

Pharmacological intervention should be considered only after treatable predisposing and precipitating factors have been managed, prior psychiatric and pain medications have been resumed, and the ICU environment has been optimized for patient comfort.

## Monitoring of Sedation and Analgesia

Pain evaluation in the ICU is generally poorly done. Patient self reporting with a visual analogue scale (VAS) is most preferred, although often difficult in the ICU setting. Table 1 shows the Critical Care Pain Observation Tool.<sup>5</sup>

Sedation scales such as the Ramsay Sedation Scale, The Richmond Agitation Sedation Scale (RASS), Sedation Agitation Score, and Motor Activity Assessment Scale are shown in Table 2 and have all been validated for use in the ICU.<sup>6</sup> Whilst such sedation scales allow better documentation, reduced sedation and analgesic use, and shorter duration of ventilation, widespread use has not yet been adopted.<sup>6,7</sup>

Objective measures of depth of sedation include the use of electroencephalograms (EEG), bispectral index (BIS) and the Narkotrend index.<sup>6</sup> None of these are commonly employed.

## Sedative and Analgesic Agents

Drugs used for analgesia and sedation in the ICU are compared in Table 3. Choices of sedative agents are determined by the underlying cause of discomfort, the sensitivity of patients to the agents and the likely length of sedation required. Optimal strategies match the patients needs with a particular drugs' pharmacokinetic and pharmacodynamic profile. The context sensitive half times indicate the change in half time clearance of a drug, when the preexisting duration of infusion is considered. During prolonged infusions, drugs are redistributed to saturate body compartments, and when stopped, clearance is prolonged.

## IV Induction Agents

Propofol had been extensively used as an ICU sedative infusion. With a high clearance, propofol sedative infusions allowed shorter times between termination of infusion and extubation. A recent meta-analysis<sup>8</sup> concluded using propofol infusion reduced duration of mechanical ventilation and length of ICU stay only when compared with long acting benzodiazepines, but not when compared with midazolam.

Side effects include myocardial depression, reduced systemic vascular resistance, hypertriglycercaemia, elevated amylase levels and green urine.



Its' use has been curtailed by the increasing awareness of propofol infusion syndrome. This results in severe metabolic acidosis and muscle necrosis, likely due to impairment of fatty acid chain oxidation and inhibition of oxidative phosphorylation in mitochondria.

Thiopentone infusions are mainly used in refractory status epilepticus or refractory intracranial hypertension. Hepatic enzyme saturability means zero order kinetics with prolonged infusions resulting in prolonged waking times, as well as myocardial depression and immunosuppression.

Ketamine infusions are used in resistant status asthmaticus. A phencyclidine derivative, it produces a dissociative anaesthesia, analgesia and amnesia. Side effects include sympathetic stimulation with increased cardiac work, and delirium.

## Benzodiazepines

Benzodiazepines bind to the GABAA ligand gated Cl<sup>-</sup> channel to produce sedation and hypnosis. Midazolam has the highest clearance, and minimal haemodynamic effects and is the most commonly used sedative infusion.<sup>3,6</sup> Concerns include increased delirium, dependence and withdrawal agitation.

## Opioids

Opioids produce analgesia, narcosis and anxiolysis. Side effect concerns include respiratory depression, histamine release, bradycardia, hypotension, nausea and vomiting and poor gastric motility. Withdrawal agitation is also a concern.

There are differences in specific agents. Morphine's histamine release contribute to increased pruritis and potential bronchospasm, compared with fentanyl. Accumulation after continuous drug infusion can lead to prolonged drug effects.

Remifentanyl is an ultrashort acting ester opioid commonly used in anaesthesia. It's metabolism is non organ dependant and is by nonspecific blood and tissue esterases to an inactive metabolite. This means it has a stable context sensitive half time (3-10 mins). Offset is therefore independent of length of preceding infusion. Studies have shown shorter weaning from mechanical ventilation and duration of ICU stay compared with other opioids.<sup>9</sup> Increased relative costs is a concern. Concerns are similar to those of other opioids and include bradycardia, hypotension and acute onset withdrawal. In addition because of rapid offset of effects, alternative analgesia may be required when infusions are stopped.

Loading dose is 1 g/kg over 1 minute. Infusion concentrations are commonly 20, 25 or 50 g/ml. Infusion rates of 0.1-0.15 g/kg/min can be continued and increased by 0.025 g/kg/min at 5 min intervals to a maximum rate of 0.2 g/kg/min.

## 2 Agonists

Dexmedetomidine is a new potent 2 agonist acting in the

locus ceruleus, causing inhibiting sympathetic stimulation, analgesia, sedation, without causing respiratory depression. Studies have shown improved weaning in patients with agitation from opioid or benzodiazepine withdrawal.<sup>10</sup> Dexmedetomidine was compared with midazolam in 375 mechanically ventilated ICU patients for up to 30 days of continuous infusion. RASS scores were kept between -1 to +1.<sup>11</sup> Riker et al. found less delirium, (54% in dexmedetomidine group vs 76.6% in midazolam group, p<0.01) in less tachycardia and hypertension, and less time on ventilators (3.7 days in dexmedetomidine group vs 5.6 days in midazolam group p<0.05). Delirium has been independently associated with cognitive impairment and 6 month mortality. Concerns include hypotension, bradycardia, and absence of approval for infusions longer than 24 hours. There is a study underway by the US NIH clinical trials group comparing dexmedetomidine and propofol for sedation of ICU patients.

Infusion concentrations are commonly 4 g/ml with a loading dose of 1 g/kg recommended over 10 minutes. Infusion rates of 0.2-0.7 g/kg/hr can be continued for 24 hours. In the study, infusions were continued up to 30 days.

## Antipsychotic Agents

Haloperidol is effective in the management of delirium and has been recommended by the SCCM guidelines.<sup>1</sup> Boluses of 1-5mg are useful in conjunction with other sedative anxiolytics. Side effects can include QT prolongation, hypotension and extrapyramidal movement tics.

## Neuromuscular Blocking Agents

Neuromuscular blocking agents are used sparingly in today's ICU. Concerns include critical illness myopathy, and awareness from inadequate sedation. Current indications are reserved for patients with difficult ventilation from high airway pressures, prevention of shivering in patients undergoing hypothermia, and malignant intracranial hypertension. Cisatracurium and rocuronium are the commonly used non depolarizing muscle relaxants, because of their relative cardiostability. Cisatracurium undergoes hoffmans degradation and similar to remifentanyl is metabolized by tissue and plasma esterases.

## Sedations Use

Although new drugs continue to become available, it is increasingly recognized that it is how sedatives are used that requires a new approach.

Choices in Usage Include:

1. Continuous infusion
2. Bolus
3. Daily stop sedation trials
4. Sleep aids
5. Sedation protocols
6. Monitoring of sedation



A number of studies have shown the benefit of daily stop of sedation trials over continuous infusions. Kress et al. demonstrated a reduction in duration of mechanical ventilation, length of ICU stay and fewer investigations to look for cause of unexplained changes of mental status.<sup>12,13</sup>

Most recently, the ABC trial randomized 335 ventilated patients to a protocol that paired spontaneous awakening trials (SATs)-ie, daily interruption of sedatives-with spontaneous breathing trials (SBTs) versus SBTs alone.<sup>14</sup> Patients in the intervention group spent more days breathing without assistance than the control group (14.7 days vs 11.6 days; mean difference 3.1 days, 95% CI 0.7 to 5.6;  $p=0.02$ ) and were discharged from intensive care (median time 9.1 days vs 12.9 days;  $p=0.01$ ) and the hospital earlier (median time 9 days vs 19.2 days;  $p=0.04$ ). More patients in the intervention group self-extubated. (16 patients vs six patients; 6.0% difference, 95% CI 0.6% to 11.8%;  $p=0.03$ ), but the reintubation rates were similar. Patients in the intervention group were less likely to die than were patients in the control group (HR 0.68, 95% CI 0.50 to 0.92;  $p=0.01$ ). For every seven patients treated with the intervention, one life was saved. (NNT 7.4, 95% CI 4.2 to 35.5) They concluded daily wake and breath trials improve outcomes and should be employed universally.

Nurse driven protocols have been validated and involve nurse assessment of:<sup>5,6</sup>

1. Sedation/Agitation Scale
2. Haemodynamic stability
3. Titration of sedation agent selected
4. Daily stop of Sedation

## Conclusions

Critically ill ventilated patients benefit from the optimization of their sedation and analgesia management. Sedation strategies must incorporate a recognition and management of causes and precipitants for pain and anxiety in ICU patients. Using sedation scales can improve sedation titration and minimize over and undersedation. Newer agents for sedation infusion

such as dexmedetomidine and remifentanyl add to the armament of the intensive care physician. The use of daily sedation interruption together with daily spontaneous wean protocols has been shown to decrease mortality in the critically ill.

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Table 1 Critical Care Pain Observational Tool

Indicator	Description	Score
Facial expression	No muscular tension observed Presence of frowning, brow lowering, orbit tightening, and levator contraction All of the above facial movements plus eyelid tightly closed	Relaxed, neutral: 0 Tense: 1 Grimacing: 2
Body movements	Does not move at all (does not necessarily mean absence of pain) Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed	Absence of movements: 0 Protection: 1  Restlessness: 2
Muscle tension	No resistance to passive movements Resistance to passive movements Strong resistance to passive movements, inability to complete them	Relaxed: 0 Tense, rigid: 1 Very tense or rigid: 2
Compliance with the ventilator	Alarms not activated, easy ventilation Alarms stop spontaneously Asynchrony: blocking ventilation, alarms frequently activated	Tolerating ventilator or movement: 0 Coughing but tolerating: 1 Fighting ventilator: 2
OR Vocalisation (extubated patients)	Talking in normal tone or no sound Sighing, moaning Crying out, sobbing	Talking in normal tone or no sound: 0 Sighing, moaning: 1 Crying out, sobbing: 2

Scores for each of the four domains are summed, with a total score of 0 to 8 [34].  
Sessler et al. Critical Care 2008 12(Suppl 3):S2



Table 2 Four Subjective Sedation Assessment Scales: A Comparison of Their Scoring

	Ramsay Scale	Sedation Agitation Scale	Richmond Agitation Sedation Scale (RASS)	Motor Activity Assessment Scale
Agitated	1 Anxious, agitated, both	7 Dangerously agitated 6 Very agitated 5 Agitated	+4 Combative +3 Very agitated +2 Agitated +1 Restless	6 Dangerously agitated, uncooperative 5 Agitated 4 Restless but cooperative
Calm	2 Cooperative, orientated & tranquil 3 Patient responds to command only	4 Calm and cooperative	0 Alert and calm	3 Calm and cooperative
Sedated	4 Brisk response to light glabella tap 5 sluggish response to light glabella tap 6 No response	3 Sedated 2 Very Sedated 1 Unarousable	-1 Drowsy -2 Light sedation -3 Moderate -4 Deep sedation -5 Unarousable	2 Responsive to touch, name, both 1 Responsive only to noxious stimuli 0 Unresponsive
Source	Ramsay MA et al. BMJ 1974;2(5920):656-9	Riker R et al. CCM 1994 ;22(3) :433-40	Sessler CN et al. AJRCCM 2002 ;166(10) :1338-44	Devlin JW et al. CCM 1999 ;27(7) :1271-5

Table 3 A Comparison of Commonly Used ICU Sedative and Analgesic Agents

Drug	Elimination	Duration	Dosing IV	Concentration	Advantages	Disadvantages	Relative Cost
Midazolam -Benzodiazepine	Cyt P450 Active metabolite	1-4h longer if elderly liver/renal failure	LD 2-5mg MD 1-10mg/hr	1mg/ml	Short acting Cardiac stable	↑Delirium Dependance Withdrawal	\$\$\$
Propofol	Conjugation	3-10 mins	MD 5-150 µg/kg/min	10mg/ml Undiluted	Short Acting Rapid offset ↓ICP ↓ wean time	Propofol infusion syndrome ↓BP, ↑lipid, amylase	\$\$\$\$
Morphine -Opioid	Conjugation Active metabolite	2-4hr ↑ if long infusion liver/renal failure	LD 2-4mg MD 1-20mg/hr	1mg/ml	Anxiolytic ↓HR, ↓RR Cheap	Resp depression, ↓BP, withdrawal, ↓GI absorbtion	\$
Remifentanil -Opioid	Tissue Esterases	10-20 mins	LD 1 g/kg- 1min MD 0.6-1.5 µg/kg/hr	20, 25, 50 µg/ml	No accumulation rapid offset ↓ wean time	↓HR, ↓BP, ↑ICP acute withdrawal	\$\$\$
Dexmedetomidine	Cyt P450 Glucuronidation	6mins ↑ in liver failure	LD 1 g/kg-10mn MD 0.2-0.7 µg/kg/hr for 24hr	2 µg/ml	Rapid offset No respiratory depression Withdrawal Mx ↓ wean time ↓ delirium	↓HR, ↓BP, Not > 24hrs expensive	\$\$\$\$\$



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## Scuba Diving

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Dr. Gloria PEI

When I was five years old and living in California, I nearly drowned in a neighbour's swimming pool. I still remember the frantic struggle to keep my head above water, my heart pounding so hard that I thought my chest would burst and the overwhelming fear and panic until I was pulled to safety. Perhaps because of this personal history, I made sure my two daughters learned to be good swimmers and to love the water. We enjoyed many beach holidays while they were growing up, but as they became more competent and adventurous swimmers, I was more likely to be found close to the shore (wearing a life vest for security) or covered with sunblock and reading at the poolside.

On one such holiday, my elder daughter took a resort scuba diving course with her father. My younger daughter was too young to participate so she and I snorkelled. From the surface we could see the two of them amongst all the beautiful fish and coral. The sun warmed our backs as we floated mesmerised by the view. It was like looking down into a giant aquarium. My elder daughter was so enthused by her first scuba experience that when we returned to Hong Kong she and her father immediately enrolled in a course to become PADI certified divers. When my younger daughter reached eligible age, it was clear that she would have to take the course alone unless I agreed to take it with her. Truthfully, given my childhood trauma, I was not at all keen and was in fact more than a little scared. However, my love and empathy for my little daughter was greater than the sum of all my fears. Besides, I did not want to be left completely behind, so the two of us signed up.

Despite my determination, the prospect of diving was stressful. I dealt with this in the same manner that most doctors face difficult circumstances: hope for the best, but prepare for the worst. My 11 year-old and I studied the course material together in the evenings after she finished her regular schoolwork and on weekends. Actually, it was fun reviewing and explaining basic gas laws, concepts of balance and buoyancy, and rudimentary lung and exercise physiology. I insisted that we also study water safety rules, underwater dangers (such as currents, venomous plants and animals, sharks, etc.) and common water-related injuries and illnesses. We both passed the written examinations without difficulty and moved onto the practical skills. Completely comfortable around water, my daughter had no trouble passing the closed water exam which was conducted in a swimming pool. For me, though, just putting on the wetsuit, which fit rather too snugly on my not-so-buffed middle-aged body, was

a huge struggle, and I found that the mask (I don't know how people can sleep with a CPAP mask) seemed to heighten the sense of tension and anxiety. Furthermore, descending underwater to scuba requires the diver to wear weights, to actively deflate a flotation device and not to kick one's finned legs to propel upward. These steps to "let go" of the surface are counter-intuitive for someone who had nearly drowned - even more so than might be expected for a person who by nature is rather cautious and has been accused by her children as being somewhat obsessive and controlling. While I really wanted to be able to dive with my little daughter and though intellectually I knew that I was prepared and perfectly "safe," I felt all my childhood fears and anxiety about drowning resurface during the closed water dive. It was really terrible.

Our teacher was incredibly patient and kind. His day-job was as an investment banker, yet he seemed to understand my difficulties. He knew that I was far beyond my comfort zone. He suggested that I just think things through and take my time. Convinced that diving was something that I really wanted to do and would enjoy, he volunteered to spend extra sessions with me to practise all the skills and help me feel more confident. I am forever grateful for his gentle encouragement and forbearance. Without his generosity and support, I might have given up at this stage. By the time we were scheduled to take the open water test in Australia, I felt I was ready.

We had been to the resort where we scheduled the open water examination before and I knew that the safety standards were very high. A dive boat took us out near Cod Hole in the Great Barrier Reef. It was a glorious, cloudless day. As we waited for our divemaster's instruction to descend, we bobbed at the ocean surface, suspended at the interface between infinite skies and the seemingly endless deep below. We were just three little specks in a vast blue universe.

The divemaster signalled us to descend. The gentle rocking of the surface waves was soon echoed by the sounds of our own breathing. The rhythm and pace of our respiration were somehow reassuring, an affirmation that we were fine. Below the surface, the waters were teeming with life. The colourful, some almost highlighter-fluorescent-hued, tropical fish were like confetti in the sunlight streaming from above. The plant life was similarly vibrant. The coral gardens were spectacular. It was all so beautiful and now my daughter and I were not just looking at, but were part



of, this fantastic aquarium. When we resurfaced at the end of our dive, my little daughter read my mind when she exclaimed, "Wow, that was great!"

My daughter and I successfully completed the exam and were PADI certified on her twelfth birthday. Luckily for us, there are many wonderful dive destinations in the region, and we try to take a dive trip every year. Our experiences have been amazing. One year, we woke up before 5 am so that we could see the humphead wrasses feed. As dawn broke, they came, maybe 50 of them, like a majestic herd of bison or a regiment of soldiers all marching in one direction. Then, suddenly, in a flash, they all turned and swam away in the direction from which they came. (This sight was so impressive, that my daughters insisted that we do it again the next morning! It was just as startling the second time.) On one occasion, my daughters and I hovered in the vortex of circling jack fish, the silver bodies swirling and enclosing us in a little piscine tornado. One of my favourite photographs of my younger daughter is of her swimming alongside a Napoleon fish as big as she was. The fish was big and friendly, like the family dog, leaning into us and allowing us to pet its body. It swam beside her until it

was time for us to return to the dive boat and then continued alongside the boat for a while. On another trip, we came across a group of 15 sea turtles resting near some barrel sponges. It was like a scene out of "Finding Nemo." As we passed near them, they began to swim. I found myself looking eye to eye with one large turtle, which perhaps had been swimming in the waters as long as I had been alive. Its eyes were clear and shiny. We have seen many sharks over the years. The sight of their natural grace and beauty do not fill one fear, but rather deep awe.

These are just some of the memories I will cherish forever and which draw me back to the waters. I decided to learn to scuba dive for the sake of my daughters, but I have benefitted far more than they have from the experience. Becoming a PADI-certified diver has been a transforming, instructive and rewarding process, and scuba diving is an activity that I now truly enjoy. In addition to being able to continue an activity with my now grown daughters, through diving, I have learned to appreciate that we are never too old to face a challenge, to overcome fears, or to learn new skills with which we can continue to explore our beautiful world.



Dermatological Quiz

# Dermatological Quiz

**Dr. Lai-yin CHONG**

MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)  
*Yaumatei Dermatology Clinic, Social Hygiene Service*



Dr. Lai-yin CHONG



*Multiple circumscribed sclerotic patches with active border at the abdomen*

A 50-year-old man developed these asymptomatic patches at his abdominal walls for six months. The lesions gradually increased in size. There were no systemic symptoms. He was otherwise well in health. On palpation, these lesions were indurated and confined to the abdominal wall. Skin scraping for fungi was negative.

### Questions:

1. What is your provisional diagnosis and differential diagnoses?
2. What investigations will you perform?
3. What are the treatment options available?
4. What is the prognosis of this disease?

*(See P. 41 for answers)*



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		<ul style="list-style-type: none"> <li>★ HKMA - Tai Po Community Network CME Lecture: Management of Skin Allergies</li> <li>★ FMSHK Officers' Meeting</li> </ul> <p style="text-align: center;"><b>1</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Clinical Ophthalmology</li> </ul> <p style="text-align: center;"><b>2</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Council Meeting</li> </ul> <p style="text-align: center;"><b>3</b></p>	<ul style="list-style-type: none"> <li>★ Joint Surgical Symposium - Latest Achievements and Developments</li> <li>★ Certificate Course on Dental Nursing in Oral Surgery</li> </ul> <p style="text-align: center;"><b>4</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Trailwalker Training Session 4</li> <li>★ HKMA/MPS Risk Management Workshop</li> </ul> <p style="text-align: center;"><b>5</b></p>
<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ HKMA Badminton Tournament</li> </ul> <p style="text-align: center;"><b>6</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> </ul> <p style="text-align: center;"><b>7</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> </ul> <p style="text-align: center;"><b>8</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ HK Neurosurgical Society Monthly Academic Meeting - Cavernoma</li> <li>★ Certificate Course on Clinical Ophthalmology</li> </ul> <p style="text-align: center;"><b>9</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ The Cosmetic Academic Exchange Workshop for BTXA (Botulinum Toxin Type A)</li> <li>★ HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2009 - New Trends in Management of Vitreo-Retinal-Macular Diseases - From Diagnosis to Treatment</li> </ul> <p style="text-align: center;"><b>10</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ Certificate Course on Dental Nursing in Oral Surgery</li> </ul> <p style="text-align: center;"><b>11</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ Certificate Course on Clinical Ethics in Practice</li> </ul> <p style="text-align: center;"><b>12</b></p>
<ul style="list-style-type: none"> <li>★ HKMA Certificate Course on Family Medicine 2009</li> </ul> <p style="text-align: center;"><b>13</b></p>	<ul style="list-style-type: none"> <li>★ Management of Drug Abusers on Public-Private Interface - Session One</li> </ul> <p style="text-align: center;"><b>14</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> </ul> <p style="text-align: center;"><b>15</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ HKMA Golf Tournament</li> <li>★ HKMA CME - Glitazone for Type 2 DM Management - Insights from Recent Outcome Trials</li> <li>★ Certificate Course on Clinical Ophthalmology</li> <li>★ Rhinitis, Sinusitis and Nasal Polyposis - Practical Suggestions for General Practitioners</li> </ul> <p style="text-align: center;"><b>16</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ FMSHK Executive Committee Meeting</li> </ul> <p style="text-align: center;"><b>17</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Dental Nursing in Oral Surgery</li> </ul> <p style="text-align: center;"><b>18</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ HKMA Trailwalker Training Session 5</li> <li>★ Certificate Course on Clinical Ethics in Practice</li> </ul> <p style="text-align: center;"><b>19</b></p>
<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ HKMA Badminton Tournament</li> </ul> <p style="text-align: center;"><b>20</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ Management of Drug Abusers on Public-Private Interface - Session One</li> </ul> <p style="text-align: center;"><b>21</b></p>	<ul style="list-style-type: none"> <li>★ HKMA/MPS Risk Management Workshop</li> <li>★ Certificate Course on Respiratory Medicine 2009</li> </ul> <p style="text-align: center;"><b>22</b></p>	<ul style="list-style-type: none"> <li>★ HKMA-Shatin Doctors Network - Certificate Course on Osteoporosis</li> <li>★ Certificate Course on Clinical Ophthalmology</li> </ul> <p style="text-align: center;"><b>23</b></p>	<ul style="list-style-type: none"> <li>★ (1) Bubbles, Bubbles, Bubbles (2) TB or not TB</li> </ul> <p style="text-align: center;"><b>24</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Dental Nursing in Oral Surgery</li> </ul> <p style="text-align: center;"><b>25</b></p>	<ul style="list-style-type: none"> <li>★ Recounting the Experience and Impact of Hong Kong Students Who Studied Medicine in War-time China</li> <li>★ Certificate Course on Clinical Ethics in Practice</li> </ul> <p style="text-align: center;"><b>26</b></p>
<ul style="list-style-type: none"> <li>★ HKMA Structured CME Programme with PMH Year 2009 (8) - i) Use of Drugs in Old Age ii) Hypertension on Old Age</li> <li>★ HKMA Tennis Tournament</li> </ul> <p style="text-align: center;"><b>27</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Respiratory Medicine 2009</li> </ul> <p style="text-align: center;"><b>29</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Clinical Ophthalmology</li> </ul> <p style="text-align: center;"><b>30</b></p>				



Date / Time	Function	Enquiry / Remarks
<b>1</b> TUE 1:00 pm 8:00 pm - 10:00pm	<b>HKMA - Tai Po Community Network CME Lecture: Management of Skin Allergies</b> Organised by: HKMA - Tai Po Community Network, Speaker: Dr. HO Hok Kung Marco, Venue: Tai Po <b>FMSHK Officers' Meeting</b> Organised by: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Miss Alice TANG Tel: 2527 8285 1.5 CME Points Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345
<b>2</b> WED 7:00 - 8:30 pm (9,16,23,30)	<b>Certificate Course on Clinical Ophthalmology</b> Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Ophthalmological Society, Speakers: Various, Venue: Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Erica HUNG Tel: 2527 8898 Fax: 2865 0345 Website: <a href="http://www.fmshk.org">http://www.fmshk.org</a> 9 CNE Points / CME/CPD Accreditation in Application
<b>3</b> THU 8:00 pm	<b>HKMA Council Meeting</b> Organised by: The Hong Kong Medical Association, Dr. H.H. TSE, Venue: HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Christine WONG Tel: 2527 8285
<b>4</b> FRI 8:00 am - 9:00 am 7:00 pm - 8:30 pm (11,18,25)	<b>Joint Surgical Symposium - Latest Achievements and Developments</b> Organised by: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Prof. William WEL, Speakers: Dr. CHAN Yu-Wai & Dr. Vivian MOK, Venue: Hong Kong Sanatorium & Hospital <b>Certificate Course on Dental Nursing in Oral Surgery</b> Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Association of Oral and Maxillofacial Surgeons Limited, Speakers: Various, Venue: Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active) Ms. Erica HUNG Tel: 2527 8898 Fax: 2865 0345 Website: <a href="http://www.fmshk.org">http://www.fmshk.org</a> 9 CNE Points / CME/CPD Accreditation in Application
<b>5</b> SAT 3:00 pm (6,7,8,9,10,11,12,15,16,17,19,20,21,22)	<b>HKMA Trailwalker Training Session 4</b> Organised by: The Hong Kong Medical Association, Venue: MacLehose Stage 6-8 <b>HKMA/MPS Risk Management Workshop</b> Organised by: The Hong Kong Medical Association, Speaker: Dr. Anne KOLBE & Dr. Jo BURNAND, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Dora HO Tel: 2527 8285 Miss Viviane LAM Tel: 2527 8452 2 CME Points
<b>6</b> SUN 2:00 pm (20)	<b>HKMA Badminton Tournament</b> Organised by: The Hong Kong Medical Association, Venue: MacLehose Medical Rehabilitation Centre	Ms. Dora HO Tel: 2527 8285
<b>9</b> WED 7:30 am	<b>HK Neurosurgical Society Monthly Academic Meeting - Cavernoma</b> Organised by: HK Neurosurgical Society, Chairman: Dr. WONG Wai Kei, Speaker: Dr. WONG Ping Hong Derek, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points (College of Surgeons of Hong Kong)
<b>10</b> THU 12:00 pm - 3:00 pm 2:00 pm	<b>The Cosmetic Academic Exchange Workshop for BXTA (Botulinum Toxin Type A)</b> Organised by: Hugh Source (International) Ltd, Venue: The Mira Hong Kong Hotel (TST), Registration: Limited seat, please book in advance (Free admission) <b>HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2009 - New Trends in Management of Vitreo-Retinal-Macular Diseases - From Diagnosis to Treatment</b> Organised by: The Hong Kong Medical Association, Speaker: Dr. CHAN Wai Man, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Mr. Sean WONG / Mr. P.C. YU Tel: 2771 6622 Miss Viviane LAM Tel: 2527 8452 1 CME Point
<b>12</b> SAT 2:15 pm - 4:30 pm (19,26)	<b>Certificate Course on Clinical Ethics in Practice</b> Organised by: The Federation of Medical Societies of Hong Kong & Hong Kong Bioethics Association, Speakers: Various, Venue: Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Erica HUNG Tel: 2527 8898 Fax: 2865 0345 Website: <a href="http://www.fmshk.org">http://www.fmshk.org</a> 6 CNE Points / CME/CPD Accreditation in Application
<b>13</b> SUN 2:00 pm	<b>HKMA Certificate Course on Family Medicine 2009</b> Organised by: The Hong Kong Medical Association, Speakers: Dr. TANG Kuen Yan Alfred & Dr. HO Chung Ping, Venue: Queen Elizabeth Hospital	Miss Viviane LAM Tel: 2527 8452 3 CME Points
<b>14</b> MON 2:00 pm (21)	<b>Management of Drug Abusers on Public-Private Interface - Session One</b> Organised by: HKMA -Tin Shui Wai, Tuen Mun and Yuen Long Community Networks and New Territories West Cluster Anti-Drug Abuse Committee of Tuen Mun Hospital, Chairman: Dr. LEE Fook Kay Aaron, Speakers: Various, Venue: Lecture Theatre, 2/F, Ambulatory Care Center, Tuen Mun Hospital, 23 Tsing Chung Koon Road, New Territories	Miss Alice TANG / Mr. Kevin CHAN Tel: 2527 8285 / 2595 6941
<b>16</b> WED 12:30 pm 2:00 pm	<b>HKMA Golf Tournament</b> Organised by: The Hong Kong Medical Association, Venue: Hong Kong Golf Club <b>HKMA CME - Glitazone for Type 2 DM Management - Insights from Recent Outcome Trials</b> Organised by: The Hong Kong Medical Association, Speaker: Dr. CHAN Wing Bun, Venue: Mongkok <b>Rhinitis, Sinusitis and Nasal Polyposis - Practical Suggestions for General Practitioners</b> Organised by: HKMA - Central, Western & Southern Community Network, Chairman: Dr. CHAN Hau Ngai Kingsley, Speaker: Dr. Paul LAM, Venue: The HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Dora HO Tel: 2527 8285 Miss Viviane LAM Tel: 2527 8452 1 CME Point Miss Alice TANG Tel: 2527 8285
<b>17</b> THU 8:00 pm - 10:00 pm	<b>FMSHK Executive Committee Meeting</b> Organised by: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345





Date / Time	Function	Enquiry / Remarks
<b>19 SAT</b> 7:30 pm	<b>HKMA Trailwalker Training Session 5</b> Organised by: The Hong Kong Medical Association, Venue: MacLehose Stage 4-6	Ms. Dora HO Tel: 2527 8285
<b>22 TUE</b> 7:00 pm - 8:30 pm	<b>Certificate Course on Respiratory Medicine 2009</b> Organised by: The Federation of Medical Societies of Hong Kong; Hong Kong Thoracic Society & American College of Chest Physicians (HK & Macau Chapter), Speakers: Various, Venue: Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Erica HUNG Tel: 2527 8898 Fax: 2865 0345 Website: <a href="http://www.fmshk.org">http://www.fmshk.org</a> 9 CNE Points / CME/CPD Accreditation in Application
<b>23 WED</b> 2:00 pm	<b>HKMA-Shatin Doctors Network - Certificate Course on Osteoporosis</b> Organised by: HKMA-Shatin Doctors Network, Chairman: Dr. Ben FONG, Speakers: Ms. Jamie LAU & Ms. Barbara CHAN, Venue: Shatin	Miss Alice TANG Tel: 2527 8285 1.5 CME Points
<b>24 THU</b> 6:30 pm - 8:00 pm	<b>(1) Bubbles, Bubbles, Bubbles (2) TB or not TB</b> Organised by: Hong Kong Thoracic Society / ACCP(HK & Macau Chapter), Chairpersons: Dr. YU Wai Cho & Dr. WONG Mo Lin Maureen, Speakers: Dr. Jones KWOK, Dr. YEUNG Yiu Cheong & Dr. YAU Pak Yuen, Venue: LG1, Lecture Room, Ruttonjee Hospital, Hong Kong	Dr. James C.M. HO / Dr. Johnny W.M. CHAN Tel: 2855 4999 Fax: 2872 5828 1 CME Point
<b>26 SAT</b> 4:00 pm - 6:00 pm	<b>Recounting the Experience and Impact of Hong Kong Students Who Studied Medicine in War-time China</b> Organised by: Hong Kong Museum of Medical Sciences Society, Chairman: Dr. LEE Kin Hung, Speakers: Dr. Joseph PAN, Dr. CHUA Sin Giap & Dr. Ramon RUIZ, Venue: Auditorium, 4/F, Li Shu Pui Block, Hong Kong Sanatorium & Hospital, Hong Kong	Ms. Cathy HUNG / Mr. Ringo NG Tel: 2549 5123
<b>27 SUN</b> 2:00 pm	<b>HKMA Structured CME Programme with PMH Year 2009 (8) - i) Use of Drugs in Old Age ii) Hypertension on Old Age</b> Organised by: The Hong Kong Medical Association, Speakers: Dr. KONG Tak Kwan & Dr. AU Kai Man, Venue: G8 Hall, Princess Margaret Hospital	Miss Viviane LAM Tel: 2527 8452 CME Points
7:30 pm	<b>HKMA Tennis Tournament</b> Organised by: The Hong Kong Medical Association, Venue: Kowloon Tong Club	Ms. Dora HO Tel: 2527 8285

## Meetings

23-25/10/2009	<b>Annual Scientific Meeting in Anaesthesiology 2009</b> Organised by: The Hong Kong College of Anaesthesiologists & The Society of Anaesthetists of Hong Kong, Chairman: Dr. S.T. TAN, Venue: The Hong Kong Academy of Medicine Building, Enquiry: ASM 2009 Secretariat, Tel: 2559 9973, Fax: 2547 9528, Email: <a href="mailto:asm2009@icc.com.hk">asm2009@icc.com.hk</a> , Website: <a href="http://www.anaesthesiology.hk">http://www.anaesthesiology.hk</a>
31/10/2009 - 1/11/2009	<b>3rd Joint Scientific Meeting of The Royal College of Radiologists and Hong Kong College of Radiologists and 17th Annual Scientific Meeting of Hong Kong College of Radiologists</b> Organised by: The Royal College of Radiologists & Hong Kong College of Radiologists, Venue: Hong Kong Academy of Medicine, Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong, Enquiry: Secretariat, Tel: 2871 8788, Fax: 2554 0739, Email: <a href="mailto:enquiries@hkcr.org">enquiries@hkcr.org</a> , Website: <a href="http://www.hkcr.org">http://www.hkcr.org</a>
1/11/2009	<b>OSHK A-Z Symposia Series "B" - Symposium: "B" Isphosphonate-Related Osteonecrosis of the Jaw and the New OSHK Guidelines on Osteoporosis Management</b> Organised by: The Osteoporosis Society of Hong Kong, Venue: Shanghai Room, Level 8, Langham Place Hotel, Mongkok, Kowloon, Enquiry: Secretariat, Tel: 2881 4295, Fax: 2159 7242
8/11/2009	<b>International Symposium on Hepatology 2009 / 22nd Annual Scientific Meeting</b> Organised by: The Hong Kong Association for the Study of Liver Diseases, Venue: Hong Kong Convention and Exhibition Centre, Enquiry: Ms. Melissa LEUNG, CMPMedica Pacific Limited, Tel: 2116 4348, E-mail: <a href="mailto:melissa.leung@asia.cmpmedica.com">melissa.leung@asia.cmpmedica.com</a>
9/1/2010	<b>Hong Kong Surgical Forum - Winter 2010</b> Organised by: Department of Surgery, the University of Hong Kong, Queen Mary Hospital & Hong Kong Chapter of American College of Surgeons, Venue: Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Forum Secretariat, Tel: 2855 4855 / 2855 4886, Fax: 2819 3416, Email: <a href="mailto:hksf@hkucc.hku.hk">hksf@hkucc.hku.hk</a> , Website: <a href="http://www3.hku.hk/surgery/forum/php">http://www3.hku.hk/surgery/forum/php</a>

## Courses

20-22/11/2009	<b>Advanced Trauma Life Support (ATLS) Student Course</b> Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons, Venue: The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Course Administrator, Tel: 2855 4885 / 2855 4886, Fax: 2819 3416, Email: <a href="mailto:hnsrg@hkucc.hku.hk">hnsrg@hkucc.hku.hk</a> , Web site: <a href="http://www.hku.hk/surgery">http://www.hku.hk/surgery</a>
20-21/11/2009	<b>Advanced Trauma Care for Nurses (ATCN) Provider Course</b> Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Course Administrator, Tel: 2855 4885 / 2855 4886, Fax: 2819 3416, Email: <a href="mailto:hnsrg@hkucc.hku.hk">hnsrg@hkucc.hku.hk</a> , Web site: <a href="http://www.hku.hk/surgery">http://www.hku.hk/surgery</a>
3-7/10/2009	<b>PALS Paediatric Advanced Life Support Course 2009</b> Organised by: Hong Kong College of Paediatricians, the Heart Institute for Children, Hope Children's Hospital, Illinois, USA & Hong Kong Paediatric Nurses Association, Speakers: Various, Venue: A & E Training Centre, Tang Shiu Kin Hospital, CME Accreditation: 12 Points for Provider Course, Enquiry: Ms. Vanessa WONG, Tel: 2871 8773, Fax: 2785 1850, Email: <a href="mailto:enquiry@paediatrician.org.hk">enquiry@paediatrician.org.hk</a> , Website: <a href="http://www.paediatrician.org.hk/entcnews.htm">http://www.paediatrician.org.hk/entcnews.htm</a> (Application starting now until August 09)
12-13/12/2009	<b>Advanced Medical Life Support (AMLS) Provider Course</b> Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons, Venue: The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong, Enquiry: Course Administrator, Tel: 2855 4885 / 2855 4886, Fax: 2819 3416, Email: <a href="mailto:hnsrg@hkucc.hku.hk">hnsrg@hkucc.hku.hk</a> , Web site: <a href="http://www.hku.hk/surgery">http://www.hku.hk/surgery</a>

### The Federation President Cup Soccer Five Tournament 2009

The Federation President Cup Soccer Five Tournament 2009 was held in Macau on the 12 July 2009. Prior to the tournament, Dr. Kingsley Chan delivered a session sharing on the "Update Treatment on Acne" on 11 July 2009 evening, which was sponsored by Stiefel Laboratories. 45 participants attended the dinner, with 17 practising doctors in Macau.

The Soccer Five Tournament was held on Sunday, 12 July 2009. There were eight participating teams, six from Hong Kong and two from Macau. They were:

- Alcon (Hong Kong) Limited (HK)
- AstraZeneca Hong Kong Limited (HK)
- Centro Hospitalar Conde de Sao Januario, CHCSJ (Macau)
- Federation Inviting Team (HK)
- Hong Kong Ophthalmological Society (HK)
- Hong Kong Medical Association (HK)
- Kiang Wu Hospital (Macau)
- Pfizer Corporation (HK) Ltd (HK)



The Champion - Pfizer Corporation (HK) Ltd



1st Runner up - Federation Inviting Team

**Invited guests officiating at the opening ceremony**  
From left to right: Dr. Jimmy Lai (Committee), Ms. Tina Yap (Committee), Dr. Susanna Lo (2nd Vice President), Dr. Raymond Lo (1st Vice President), Dr. Dawson Fong (President), Dr. Lee Pui I (President of Macau Physician Association of Public Hospital), Dr. Tse Hung-hing (President of HKMA), Dr. Liu Wing-hong (Co-chairmen), Mr. Nelson Lam (Co-chairmen), Dr. Kingsley Chan (Co-chairmen)



2nd Runner up - AstraZeneca Hong Kong Limited



The tournament started as early as 8.30am. After rounds of 16 matches, it finished at 5.40pm. Congratulations to the winning teams:

- 🏆 **Champion - Pfizer Corporation (HK) Ltd**
- 🏆 **1st Runner up - Federation Inviting Team**
- 🏆 **2nd Runner up - AstraZeneca Hong Kong Limited**

The two Top Scorers go to Mr. Nicholas Chan of the Pfizer Corporation (HK) Ltd team and Mr. Alex Lam of the Federation Inviting Team.

The event ended with a cocktail party and award presentation ceremony.



**Top Scorers**  
From left to right:  
Mr. Nicholas Chan (Pfizer Corporation (HK) Ltd),  
Dr. Liu Wing-hong (Co-chairmen),  
Mr. Alex Lam (Federation Inviting Team)



## Answer to Dermatological Quiz

1. Morphoea (localized scleroderma)  
The differential diagnoses in this patient included mycosis fungoides, tinea corporis and erythema annulare centrifugum. Morphoea is an inflammatory disease primarily affects dermis and subcutaneous fat of skin, resulting in sclerosis and deformity. It is a distinct entity with a clinical course completely different from systemic scleroderma, though histologically the two conditions are identical in the skin lesions. Morphoea occasionally can be generalized and simulate diffuse scleroderma, but systemic involvements are absent. Raymond's phenomenon is also absent in morphoea but present in 90% of systemic scleroderma.
2. Skin biopsy for histopathology should be done to confirm the diagnosis.
3. Various topical medications have been used but the results are unsatisfactory in general. These include topical or intralesional corticosteroids, topical calcineurin inhibitors, topical vitamin A and vitamin D analogues. For generalized morphoea, UVA1 or bath PUVA phototherapy seems promising. For rapidly progressive disabling disease, weekly methotrexate combined with pulsed therapy of corticosteroids has recently been advocated by some workers.
4. With the absence of systemic involvement, morphoea is not fatal as in its systemic counterpart. However, it does cause significant morbidity with the resulted disfigurement, or functional disabilities due to contractures. In severe lesions, the underlying muscle and bone may be involved. The disease often progresses for several years before finally regresses and burns out.

### Dr. Lai-yin CHONG

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