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Mechanical Ventilation in ARDS: Volume or Pressure Limited

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Alveolar recruitment is an important objective in the ventilatory management of acute respiratory distress syndrome (ARDS) patients. The static lung mechanics are considered state of the art in spite of the fact that they only provide a narrow view and do not represent the mechanical behaviour of the lung during on-going tidal ventilation. Nevertheless, a dynamic lung mechanics point of view is still more difficult make a good interpretation. Both, volume and pressure are the inflection of the points of view for patients with ARDS. Several studies has demonstrated that using small tidal volume (V_T) improve the mortality rates in patients with ARDS, but when we are using pressure limited, also is possible, we are using small tidal volume, in addiction to the severe an altered compliance presents in this patients. But, which is the difference? Is it better to control the volume or the pressure, or both? The reduction of V_T and end-inspiratory plateau pressure is therefore recommended in order to limit lung distending pressure.

The pressure-volume (P/V) curves of the respiratory system has contributed to a better understanding of the complex rules governing alveolar recruitment and derecruitment, playing a key role in the concept of lung protection.

A future and widely vision of the problem, should be considered that the “small tidal volume is not only the more important” and perhaps “how the flow could be given during the ventilatory support”.

This lecture talking about the recent advances concerning the use of pressure-volume (P/V) curves to optimize lung recruitment in ARDS patients under mechanical ventilation, and which is the conduct to consider based on the best decision.

Acute Cor Pulmonale

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Right heart dysfunction is frequently encountered in the intensive care setting. Although it may occur as a result of a primary cardiac problem such as a myocardial infarction, more commonly it is a manifestation of underlying pulmonary disease. Examples would include: pulmonary embolus, ARDS, left heart problems resulting in marked elevation of the left ventricular end diastolic pressure. The gross manifestations of acute cor pulmonale are very evident clinically but lesser degrees are difficult to diagnose, particularly in the presence of multi-organ failure where significant peripheral oedema is present. Invasive techniques such as pulmonary artery catheters are very helpful in identifying elevated pulmonary artery pressures. Echocardiography has the advantage of being non-invasive, more readily applied and in the long term less expensive. The presence of intracardiac masses suggestive of thrombi may assist in the decision as to whether to thrombolise the patient.

Available therapies for the treatment of acute cor pulmonale are far from ideal. Where the obstruction downstream can be relieved (such as in the case of a massive pulmonary embolus, or ventilatory techniques that result in increased pulmonary artery pressure) can be relieved then it should be undertaken. Often the emphasis is on attempting dilatation of the pulmonary vasculature. Many of the drugs commonly used in systemic hypertension are not so efficacious in pulmonary hypertension. Bosentim, sildenafil, prostacyclins and nitric oxide all have a role in the critically ill patient. Augmentation of right ventricular contractility can be useful. Inotrope agents including epinephrine, norepinephrine, and dobutamine are often helpful.

Status Asthmaticus in Children

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Asthma affects 10% of children and causes 25% of school absenteeism. Hospitalization cause by asthma attack has tripled, and accounts for 5% of PICU admissions. Death rate has increased in the last 15 years.

Status asthmaticus is an asthma attack refractory to initial therapy. Indicators of status asthmaticus: PEFR <150 L/minute or <50% predicted; pulse oximetry <91% on room air; tachycardia (HR >120) and tachypnea (RR >30).

Pathophysiology of asthma is primarily an inflammatory disease, which involved smooth muscle spasm, airway edema, and mucous plugging. Activated mast cells and lymphocytes which produce pro-inflammatory cytokines (histamine, leucotriene, PAF) increased in asthmatics airway and bloodstream. In status asthmaticus there is irritable and damaged airway caused hypersecretion, epithelial damage with exposed nerve endings, hypertrophy of globet cells and mucus glands leads to obstruction of the airway triggered by allergens, infections, irritants including smoke, exercise, emotional stress, GE reflux, drugs, and other factors. Obstruction of the airway can be compensated with hyperinflation, normocapnea and decompensated with severe hyperinflation and hypercapnea.

Clinical manifestation of status asthmaticus: cough, wheezing, increased work of breathing, anxiety, restlessness, and oxygen desaturation.

Complications of status asthmaticus are increased left ventricular load resulting in risk for pulmonary edema, and right ventricular load caused by hypoxic pulmonary vasoconstriction and lung hyperinflation. Evidence of pulsus paradoxus correlates with severity. Metabolic acidosis occurs because of V/Q mismatch, increased work of breathing, and dehydration that leads to accumulation of lactates and ketones.

Management of status asthmaticus:

Conventional: using β-agonists, steroids, anticholinergics; advanced: mechanical ventilation (pressure limited ventilation, TV 8-12 ml/kg, short Ti, rate 8-12/min with permissive hypercapnea), ketamine, inhalation anesthetics; high flow oxygen, fluid therapy (most of asthmatics are dehydrated, so rehydrate to euvolemia). SIADH may be common in severe asthma. Antibiotics are not routinely indicated.

Dietary Protein Supplement in Liver Disease: Soy Protein vs Casein Protein

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Objective

To determine the effects of soy and casein protein supplement on nutritional status, vitamin B1 and vitamin B2 level, and incidence of hepatic encephalopathy in stable cirrhotic patients.

Methods

Twenty–two stable cirrhotic patients divided into 2 groups: Group I (n=10) and group II (n=12). Their ages range 27-70 years and having ideal body weight less than 100% and/or prealbumin less than 15 mg/dl. Group I and group II received casein and soy protein supplement in addition to regular diet respectively Formula with casein protein containing 32 g of carbohydrate, 5.5 g of fat,10 g of casein protein and 210 Kcal. Formula with soy protein containing 32.5 g of carbohydrate, 5.3 g of fat,10 g of soy protein and 210 Kcal. Each subject underwent supplement formula daily for 4 weeks. Physical examination, subjective global assessment (SGA), 24-hr dietary recall, anthropometry, bioelectrical impedance (BIA), arterial NH_3 level, number connection test (NCT), electroencephalography (EEG), prealbumin and vitamin level (erythrocyte transketolase activity [ETKA]

and thiamine pyrophosphate effect [TPPE]), erythrocyte glutathione reductase activity (EGRA) and activity coefficient (AC), and twenty-four hour urine creatinine height index (CHI) were taken on day 1 and day 28.

Results

There were improvement of nutritional status and vitamin levels after protein supplement in both groups, indicated by subjective global assessment (SGA) ($p < 0.02$) and no vitamin deficiency ($p < 0.05$). There was not significantly difference in others nutrition assessment parameters (anthropometry, BIA, 24-hr dietary recall, CHI, albumin and prealbumin levels). The incidence of clinical hepatic encephalopathy, arterial NH_3 level, NCT and EEG grading were not significantly difference between protein supplement of casein or soy protein in 2 groups.

Conclusion

Protein supplement improve nutritional status of stable cirrhotic patients whatever casein or soy protein supplement. The sensitive parameter for assessment of nutritional status is subjective global assessment (SGA) and vitamin levels.

Nutrition in Acute Pancreatitis

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Acute pancreatitis (AP) is a hypercatabolic state. Patients with severe acute pancreatitis may require 2000-2500 Kcal/day, of which 50%-60% may come from glucose, 15%-20% from protein and 20%-30% from lipids. In the vast majority of patients with mid to moderate AP (70%-80% of all AP patients) regular oral feeds can be started in 3-4 days and hence there is no need for any special feeds in them. On the other hand, in patients with severe AP (20%-30%) parenteral nutrition may have to be given as a supplement, especially if the patient develops MODS or remains hemodynamically unstable or has ileus and is unable to tolerate oral feeds. As soon as the patient stabilizes, the attempt should, however, be done to switch to enteral feeding.

Comparisons of total parenteral nutrition (TPN) vs enteral feeding in AP have shown superiority of enteral feeding in many ways, most importantly a decreased incidence of infection in the necrotic pancreas. Other advantages of enteral feeding include easier management, lesser complications and lower cost. Enteral feeding is therefore being increasingly favoured in severe AP. Traditionally that has been done through nasojejunal feeding but lately the trend is to give nasogastric feeding because of a few recent studies showing no difference in tolerance and efficacy between nasojejunal and nasogastric feeding. Certain nutrients may be particularly useful in specific situations. For example, immuno-nutrition provided parenterally has been shown to result in earlier resolution of severe AP. Similarly, addition of probiotics (Lactobacillus plantarum) to enteral feeding may prevent the occurrence of infection in pancreatic necrosis.

Hyperglycemia: The Probable Culprit after All These Years

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Stress-induced hyperglycemia is a consequence of critical illness, myocardial infarction, congestive heart failure, cardiopulmonary bypass surgery, global and focal cerebral ischemia, head injury, burns and major surgical procedures. Frequently, stress hyperglycemia is accompanied by insulin resistance (IR). Accumulating evidence links the poor outcome of these occurrences to hyperglycemia. Therefore, much attention has been given in recent years to treatment of the hyperglycemic condition, specifi-

cally through intensive insulin therapy. Especially where critically ill patients are concerned, calls have been sounded to consider blood glucose concentration as part of their illness severity assessment. The prevailing general recommendation for surgeons and intensivists is to vigorously monitor and maintain euglycemia in their patients via the administration of insulin or the combination of glucose-insulin-potassium (GIK) solution. Nevertheless, despite the fact that the observed hyperglycemia in all the above-mentioned conditions is recognized as induced by stress, the recommendation is to treat the outcome rather than its cause. Should the title of this presentation be "Is hyperglycemia the probable culprit after all these years?" At least one recent animal study may answer this question negatively.

Haemodynamic Monitoring in Septic Shock

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Sepsis and multiple organ dysfunction syndrome account for most deaths in the intensive care unit, and these patients place an enormous burden on all hospital services. Although the exact pathophysiology of multiple organ dysfunction syndrome is not yet known, alterations in systemic hemodynamics, organ perfusion and tissue microcirculation resulting in tissue hypoxia appear to play a key role in the onset and maintenance of this syndrome. Optimal monitoring of the critically ill ICU patient remains a challenge and controversy continues as to whether the patient will profit from a more aggressive approach to monitoring.

All are agreed, however, that simply monitoring will not improve the patient's condition – monitoring is not the same as treatment.

Monitoring of cardiac function

The assessment of ventricular function is based on the measurement of both volumes and pressures. By relating changes in left ventricular volume or pressure to time during phases of the cardiac cycle, indices of contractility can be generated. The difficulty of evaluating cardiac performance is reflected by the number of hemodynamic variables, which are thought to be indicators of myocardial function.

The most widely accepted technique for measuring cardiac output is the thermodilution method using a pulmonary artery catheter and a bedside microprocessor. This technique is easy and without risk of indicator accumulation and can be carried out multiple times in the critically ill. Newer catheters have been developed which can measure cardiac output continuously by thermodilution. The pulmonary artery catheter revolutionized monitoring in ICU and significantly contributed to a greater understanding of cardiac physiology in the critically ill. However, it has its complications and critics claim that its use does not alter outcome and other less invasive forms of monitoring should be used instead. Cardiac output can be measured non-invasively by transthoracic electrical impedance, trans-oesophageal Doppler sonography or by pulse contour analysis of the peripheral arterial waveform. Results from these other techniques are controversial with some groups finding close agreement of various techniques with the PA catheter while others find little agreement and the techniques unreliable.

Measurement of PAOP does not always reflect end-diastolic volume. The CVP and PAOP parallel each other with a high degree of correlation in the patients with EF >50% but in patients with severely impaired myocardial function this correlation is lost. However, if measurement of an index of filling pressure is required then the pulmonary artery catheter is realistically the only monitor capable of routine use in the ICU.

Mixed venous oxygen saturation

Continuous or intermittent monitoring of venous oxygen saturation is another adjunct to hemodynamic monitoring of the critically ill patient. The advantage of this technique is the ability to realise immediate indications of changes in the oxygen supply to demand ratios. Normal values range between 70 and 75% and a linear correlation has been demonstrated between SvO_2 and cardiac output. Clearly, however, SvO_2 measurement only gives global impressions – a normal value would not, for instance, rule out an impaired oxygen supply to an individual organ.

Monitoring organ perfusion

Inadequate tissue perfusion and oxygenation are likely to contribute to the development of organ failure and increased mortality in the critically ill. However, actually monitoring this has proved difficult and the measures are often insensitive. Essentially methods to detect tissue dysoxia and oxygen debt can grossly be subdivided into two groups: techniques directed at the assessment of oxygenation at the systemic level; and monitoring techniques for measurements at the organ level. Examples include tonometry (usually gastric), near infrared spectroscopy and tissue oxygen tension. Blood lactate concentrations in excess of 2 mmol/l are generally considered a biochemical indicator of inadequate tissue oxygenation. However, a number of mechanisms other than impaired tissue oxygenation may cause an increase in blood lactate, including an activation in glycolysis, reduced pyruvate dehydrogenase activity, or liver failure. The presence of elevated lactate levels should nevertheless prompt the clinician to suspect inadequate circulatory status.

Conclusions

There are many monitoring instruments available and there have been many developments in both monitoring and our understanding of cardiac physiology in the critically ill. However, what is the gold standard for hemodynamic monitoring? There is no doubt that the use of hemodynamic monitoring devices yields additional information. However, many of these devices may confuse and mislead. The major issue is whether such monitoring has an impact on patient outcome. In this regard, it has never been shown that a specific hemodynamic monitoring technique improves outcome. There is the risk that all these techniques may delay or prolong what could otherwise have been a quick, simple and safe procedure, and they may render the procedure much more expensive. Nevertheless, in the critically ill ICU patient there is a need for something, which indicates the adequacy of the patient's hemodynamic status. We still await this ideal monitor.

Metabolic Response to Surgery

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The response to surgical trauma is a well-established phenomenon, known as 'the metabolic response', involving several metabolic, endocrinologic and inflammatory systems. The most studied response to the many different surgical procedures is the reduction in insulin efficacy, known as insulin resistance (IR) and its accompanying increase in blood glucose level or hyperglycemia. A statistical analysis by Thorell *et al*. found that post-surgical IR is a marker of surgical stress and an independent predictor of the variation in the duration of hospital stay. Conversely, one could surmise that a lower postoperative IR indicates improved recovery from surgery. Past and present efforts to reduce the adverse effects of the metabolic response to surgery include preoperative, perioperative and postoperative treatment modalities. There are both benefits and drawbacks for several of these modalities that should be considered, especially when specific information from an animal model of trauma is considered.

Fluid Management in ARDS

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Pulmonary edema resulting from increased capillary permeability is a hallmark of acute lung injury and ARDS and worsens as the intravascular hydrostatic pressure rises and oncotic pressure falls. The optimal fluid management of acute lung injury is not settled. The usual practice is wide-ranging and there are risks and benefits to be assessed with either strategy – conservative versus liberal fluid management. A recent large multicenter trial has now provided us with the evidence on which to base our practice.

Results

Eleven thousand and five hundred twelve patients were screened and 1,001 randomized to the two fluid replacement strategies – 503 assigned to conservative fluid management and 498 patients assigned to liberal fluid management. The target ranges of CVP and PAOP used in this study were 10 to 14 mmHg and 14 to 18 mmHg in the liberal strategy group and 4 mmgh to 8 mmHg and PAOP less than 8 mmHg in the conservative fluid strategy group respectively.

The two groups were similar at baseline. The mean time from admission to the ICU to the first protocol instruction were the same at approximately 42 hours. Patients in the conservative group received furosemide more frequently than did patients in the liberal group, whereas patients in the latter group more often received a fluid bolus. During the study, the seven-day cumulative fluid balance was -136±491 in the conservative group as compared with 6992±502 ml in the liberal group ($p < 0.001$). For patients who were in shock as baseline, the cumulative seven-day balance was 2904±1008 ml in the conservative group and 10,138±922 ml in the liberal group. Intravascular pressures declined in the conservative group but remained essentially unchanged in the liberal group.

The conservative fluid strategy group had better lung injury scores and oxygenation indexes, as well as lower plateau pressures and levels of PEEP. There were no significant differences in any of the biochemical or blood gas measures.

The in-hospital death rate during the first 60 days was 25.5% in the conservative strategy group and 28.4% in the liberal strategy group ($p=0.30$). The conservative group had more ventilator free days and ICU free days during the first 28 days of the study. There were no significant differences in the number of failure free days for other organs.

Other strategies to reduce pulmonary edema

Alveolar fluid clearance is an important function of the alveolar epithelium but has never been systematically characterised in large groups of patients with either ALI or ARDS. One study has suggested that net alveolar fluid clearance was impaired (<3%/h) in the majority of patients (56%) and the maximal clearance rate was only observed in 13% of patients. A small trial of inhaled beta adrenoceptor agonists suggest that clearance may be improved by including this in the treatment strategy. However, the observational study showed no difference in edema clearance depending on either endogenous or exogenous catecholamines.

Conclusions

Fluid strategy did not alter outcome in terms of 60-day mortality but a conservative strategy was associated with improved lung function and shortened the duration of mechanical ventilation and intensive care without increasing nonpulmonary organ failures. These results are consistent with those obtained in animal studies, which have suggested improved lung function with diuretics and fluid restriction. In addition, they are compatible with observational studies in patients.

Sepsis: Empiric Antibiotic Therapy

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Sepsis is systemic inflammatory response syndrome (SIRS) due to an infection which induces a cascade of deranged inflammatory responses, often resulting in multiorgan dysfunction. SIRS is identified when a patient has two or more of the following criteria: 1) fever (>38 ^{0}C) or hypothermia (<36^{0}C); 2) tachycardia (heart rate >90/min); 3) tachypnea (respiration >20/min, or minute volume >10 L/min if mechanically ventilated) or $PaCO_2$ <32 mmHg; and 4) white blood cell count >12,000/ul or <4,000/ul.

Severe sepsis is sepsis associated with organ dysfunction, hypoperfusion or hypotension (systolic BP <90 mmHg or a 40 mmHg decrease below baseline systolic BP). Septic shock is severe sepsis plus hypotension despite adequate fluid resuscitation. Sepsis is the most common cause of death in most ICUs worldwide. The mortality rates for severe sepsis ranged 30% to 50%, and for septic shock 50% to 60%.

Management of severe sepsis and septic shock consists of resuscitation, investigation of the cause of sepsis, definitive therapy and adjunctive therapy. Definitive therapy for sepsis consists of source control and antibiotics. Look for a septic focus that may be amenable to eradication such as drainage (surgical or radiology/ultrasound guided percutaneous drainage) of ab-

scess, debridement of infected necrotic tissue, removal of potentially infected devices (e.g. central venous catheter) and surgery (e.g. perforated bowel).

A prompt and adequate antibiotic treatment is life saving in critically ill patients admitted to the ICU with sepsis (Table 1). A study in ICU showed that 78.9% of the 2154 septic shock patients received effective antimicrobial therapy only after the onset of recurrent or persistent hypotension. Despite that fact that each hour delay in antibiotic administration over the ensuing 6 hours was associated with an average decrease in survival of 7.6%, only 50% of septic shock patients received effective antibiotic therapy within 6 hours of documented hypotension.

Selection of appropriate antibiotic therapy depends on the likely pathogens, site of infection, Gram's stain results, local flora and susceptibility patterns, and co-morbidities. In addition, the tissue penetration into the suspected septic source and adverse effects of each antibiotic should be considered. Aminoglycosides and glycopeptides (e.g. vancomycin) have relatively poor tissue penetration and are nephrotoxic. Most agents have poor CNS penetration, except when the meninges are inflamed.

Consider combination therapy for immunocompromised or neutropenic patients and certain pathogens e.g. Pseudomonas aeruginosa. The previous use of antibiotic is a key factor to broaden the empirical regimen to cover multiply resistant strains. Non-bacterial infectious pathogens are uncommon in most ICUs but may vary depending on geographic location and host susceptibility. Fungal infection should be considered in the presence of predisposing factors such as malignancy, neutropenia, broad-spectrum antibiotic therapy, parenteral nutrition, severe burns, organ transplantation, or central venous catheter.

Review empirical broad-spectrum antibiotic regimen after 48-72 hours, based on microbiological results and clinical response. Use a narrow spectrum antibiotic to prevent the development of resistance, to reduce toxicity and to reduce cost. The duration of therapy should typically be 7-10 days and guided by clinical response. Stop antibiotic therapy immediately if the etiology is determined to be non-infectious.

A recent study on patients admitted to the ICU for sepsis showed that inadequate initial empirical antibiotic therapy was associated with a higher 28-day, 60-day, and in-hospital mortality rates, although early mortality rate (<3 days) was unaffected. Factors associated with early mortality were immunosuppression, chronic cardiac failure, and renal, respiratory or hepatic failure within the first 24 hours in the ICU.

Table 1. Empirical antibiotic therapy for patients admitted to ICU with sepsis

Community acquired	Hospital acquired
Abdomen or pelvis	
• Amoxicillin-clavulanate + aminoglycoside	• Piperacillin-tazobactam/imipenem + aminoglycoside + antifungal (optional)
• Metronidazole/clindamycin + aminoglycoside	
• Piperacillin-tazobactam + aminoglycoside (optional)	
Central nervous system (meningitis)	
• Ceftriaxone + vancomycin (optional) + ampicillin (optional) + acyclovir (optional)	
Pulmonary	
• Ceftriaxone + macrolide/fluoroquinolone	• Ceftazidime/cefepime + fluoroquinolone + aminoglycoside (optional)
• Ceftazidime/cefepime + fluoroquinolone (with structural lung disease)	
Soft tissue	
• Amoxicillin-clavulanate + aminoglycoside	• Piperacillin-tazobactam/imipenem + vancomycin
• Piperacillin-tazobactam + aminoglycoside (optional)	
Urologic	
• Ceftriaxone + aminoglycoside	• Ceftazidime/cefepime/piperacillin-tazobactam + aminoglycoside
Unknown origin	
• Ceftriaxone/ceftazidime/cefepime + aminoglycoside	• Ceftazidime/cefepime + aminoglycoside + vancomycin (optional)
Catheter	
• Vancomycin + ceftazidime/cefepime + antifungal (optional)	
Neutropenia	
• Ceftazidime/imipenem/cefepime/piperacillin-tazobactam/ceftriaxone + aminoglycoside + vancomycin	

Clinical Uses of Probiotics in Gastrointestinal Diseases

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Gut flora has been shown to be responsible for the stimulation and modulation of the immune system functions, fermentation of dietary waste and endogenous mucins, energy recovery through the generation of short-chain fatty acids, and protection of the gut from colonization and invasion by pathogens (barrier effect). These healthful bacteria are called probiotics and the indigestible dietary and starchy food items, which promote the growth of gut flora, are called prebiotics. Pro and prebiotics have been suggested as being of therapeutic use in a variety of conditions but reliable evidence based support for their beneficial effect is available only for acute Rotavirus diarrhea, acute infantile diarrhea, antibiotic associated diarrhea, traveler's diarrhea and chronic pouchitis. There is also a reasonably good support for the usefulness of probiotics in maintenance of inflammatory bowel diseases, particularly ulcerative colitis, and in prevention of allergic manifestations in children.

Whilst the clinical utility of pre and probiotics is being appreciated issues with regard to the type and load of bacteria to be used and the duration for which they should be given remain to be determined. Similarly, safety issues in immunocompromised patients remain to be addressed.

Transport and CPR of Critically Ill Patients with Contagious Diseases

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During the severe acute respiratory syndrome (SARS) pandemic in 2003, 21% of victims were healthcare workers (HCWs). The global case fatality of SARS was 9.6% (774/8096). As for avian influenza A (H5N1) in human, 228 cases have been reported from 2003 until 20 Jun 2006, with an alarmingly high global mortality of 57%. Fortunately, human-to-human transmission was limited and required very close contact with an infected person.

The World Health Organization recommends droplet and contact precautions (Tables 1 & 2) as the minimum level of precautions to all patients in all healthcare facilities to ensure a high level of protection to patients, HCWs and visitors.

Table 1. Standard precautions for all patients

1. Hand washing and antisepsis (hand hygiene)
2. Use of personal protective equipment (PPE) when handling blood, body substances, excretions and secretions
3. Appropriate handling of patient care equipment and soiled linen
4. Prevention of needlestick/sharp injuries
5. Environmental cleaning and spills-management
6. Appropriate handling of waste

Table 2. Appropriate PPE during procedures and patient-care activities on infectious patients that may generate splashes or sprays of blood, body fluids, secretions or excretions

1. High-efficiency masks where possible; alternatively, use surgical mask.
2. Clean, non-sterile gloves when entering patient's room.
3. Clean, non-sterile long-sleeved cuffed gown when entering patient's room if envisaging substantial contact with patient, environmental surfaces or items in patient's room.
4. Face shield or goggles

Given the high mortality of avian influenza A (H5N1) and the possibility of virus mutation that could lead to efficient human-to-human transmission, the highest level of precautions should be taken. Hence, additional airborne precautions, involving the use of high efficiency masks (at least as protective as US NIOSH-certified N95) and a negative pressure room if available, should be adopted.

In the event of emergency endotracheal intubation or cardiac pulmonary resuscitation (CPR) when there might be insufficient time to put on full PPE, including a powered air purifying respirator if available, experience from Singapore has shown that the use of high filtration N95 masks together with gloves, gowns and goggles offered sufficient protection. Adequate sedation and muscle relaxant should be prescribed to patients requiring endotracheal intubation and bronchoscopy to minimize cough that may lead to droplet dispersion.

A two-in-one filter consisting of a bacterial/viral filter and a heat and moisture exchanger should be attached between flexitube and Y-connector of the breathing circuit to filter out pathogens. A closed-suction system should be used. To prevent airflow from the ventilator aerosolizing the droplets, ventilator should be always put on 'standby' mode before disconnection of ventilatory circuit. Venturi masks, nebulizers and non-invasive ventilation should all be avoided.

Infectious patients needing transportation should put on a surgical mask to trap any droplets if they are breathing spontaneously. HCWs should wear full gown with gloves and mask when transporting infectious patients.

Erythromycin as A Prokinetic Agent

Ana L. Huerta-Alardín

Erythromycin is a macrolide antibiotic that has been clinically used since 1952. It was at first isolated from an actinomycete in a soil sample from the Philippines. In the 1970s, motilin, a peptide gastrointestinal hormone, was found to stimulate motor activity in the upper gastrointestinal tract in canines, and later associated with the occurrence of antral migrating motor complexes (MMCs) both in animals and humans. It was suggested then, that there were two subtypes of motilin receptors on enteric neurons and on the antral smooth muscle, as well as other sites like the colon. On the 1980s, it was first demonstrated by Itoh *et al.*, in a canine model, that erythromycin induced interdigestive migrating contractions in the small intestine, and later on confirmed by Peeters *et al*., that erythromycin was a motilin receptor agonist in human digestive tract. Erythromycin in lower doses, binds to the neural motilin receptor to induce MMCs, and in higher doses (antibacterial doses), erythromycin binds to the muscle receptor to stimulate strong antral contractions. In the clinical scenario, erythromycin was first reported being useful in diabetic gastroparesis. In critically ill patients receiving mechanical ventilation, motility is often impaired, causing delay in drug absorption, as well as duodenogastric reflux leading to colonization of the stomach by enteric Gram-negative pathogens, which is a frequent finding in these patients. Recent studies in mechanically ventilated patients have evidenced that intravenous erythromycin increases indices of antral motility and accelerates gastric emptying, as well as being an excellent aid in success of early enteral nutrition. On trauma patients, intravenous erythromycin reduced delayed gastric emptying during the first 48 hours of enteral feedings, without affecting the rate of nosocomial infection. This agent has also been used in preterm neonates suggesting that should only be reserved for high risk neonates with persistent and severe feed intolerance. Erythromycin has been related with antibiotic resistance, as well as with cardiac dysrhythmias. All the recent data suggest that erythromycin as a prokinetic agent should be used cautiously in selected patients, and had been useful in mechanically ventilated and trauma patients.

Effective Tube Feeding of Bedridden Elderly

Ana L. Huerta-Alardín

Beyond the intensive care unit, an increasing number of patients with swallowing disorders secondary to neurologic injury or degenerative neurological disorders are surviving for prolonged periods with tube feeding. Nowadays, it is a clinical challenge

to asses correctly the nutritional requirements and to choose correctly the strategy for nutrition on these patients. In our review, we did not intended to address any ethical issue regarding long-term feeding in the elderly, but we encourage physicians in and out the intensive care unit to be aware of their patients' wishes in relation to the use of long-term tube feeding before initiating any treatment. The elderly patients that require tube feeding must be assessed thoroughly before and during the use of enteral nutrition. The assessment should be integral, evaluating the functional and nutritional status. We should work as a team with several other health care providers in this difficult job, including consultations with physical therapy to evaluate physical status, as well as speech pathology for the correct selection of patients that can or cannot tolerate food orally. We stress the importance of ongoing assessment due to changes in cognition that should trigger reassessment of swallowing function. The role of the nutritionist is central, identifying nutritional risk factors, such as weight loss, gastrointestinal disorders, multiple pharmaceutical agents, and recent medical or surgical illness. Weight loss has been established as a predictor of mortality. In the patients requiring tube feeding, weight loss is extremely common, even when nutritional requirements are being correctly provided. This has been explained by decreased mobility causing atrophy of muscles, decreasing muscular mass. Laboratory values are also helpful; being albumin and cholesterol levels two of the most important, and studied in the past. Studies have showed that hypoalbuminemia and hypocholesterolemia are highly correlated with dead and the presence of pressure sores. Other important aiding laboratory values are glucose, sodium, BUN and creatinine, which give the physician and idea of protein status as well as hydration status. The correct selection of the feeding tube is also crucial, in patients that have been anticipated to use long-term feeding, have been beneficiated with the use of percutaneous endoscopic gastrostomy, due to decreased complications and cost. The formula selection depends on patient's factors, estimating nutrient needs, fluid requirements and tolerance, the presence of organ failure, stress, metabolic disorders and gastrointestinal function. The prevention of complications is the key for the efficacy of nutritional management in bedridden patients. One year-mortality for tube-fed elderly ranges from 30-40%, complications account for a great contribution to mortality. Complications include aspiration, self-extubation, gastrointestinal complications, diarrhea, constipation, and metabolic derangements. We should be aware of the long-term benefits, complications and outcomes of tube feeding elderly bedridden patients, and constant evaluation of the patient's functional status should be periodically performed. This is the best chance to provide chronic tube feeding safely and effectively.

Ethical Issues in Organ Transplantation

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Clinical organ transplantation has been recognized as one of the largest events in medical history. Until 50 years ago, failure of a vital organ such as kidney, liver or heart usually implicated immeasurable suffering and death for the patient. Organ transplantation is an option for giving the gift of life to patients with failure of vital organs. This practice requires the participation of other fellow human beings and of society by donating organs from deceased or living individuals. This review deals with ethical and moral issues generated with advances in organ transplantation, as well as the process of organ donation in the intensive care unit. The very well known gap that exists between organ supply and organ demand has been divulged by transplant professionals; stressing the situation of patients waiting on lists for transplantation, and the increasing number of deaths while waiting. These events have raised many volunteers for donation, including minors. It has also led to the practice of organ sale for financial gains and the exploitation of the poor for the benefit of the wealthy. There have been recent advances in immunology that have led to new options for consideration, such as xenotransplantation, which supports the usage of animal organs. Additional ethical implications have risen with the conception of this practice. This analysis intended to discuss ethical and moral issues that current advances in organ transplantation have generated. Another important situation we wanted to center our attention on is the moral implications and the process of organ donation in the intensive care unit; the approach by which the critical care physicians discuss organ donation with families of critically ill patients, and how to make it part of good end of life care. All these ethical dilemmas have taken many physicians and ethicists to come out with new solutions by providing better care and counseling with informed consent to the family and showing respect to the body of the deceased and the exercise of compensation for the cadaver donor funeral, travel and other expenses. Other ethical discussions include the certifying of death of the cadaver donor and the allocation of organs. Currently other debates have emerged that include directed versus anonymous donation, in case of living donors, and the organ sale of transplants, as well as the priory mentioned financial incentives or compensations for organ

donations. If we want clinical transplantation to be used as intended it should be fully beneficial and life-saving, the entire team involved in the process should respect and consider the best interest of the patient and honor the ethical values of society and avoiding personal gain, or financial benefits.

The Obese Patient in the Intensive Care Unit

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Obesity is a serious disorder resulting in significant impairment of health. Overweight and obese adults are at in increased risk of morbidity and mortality from many acute and chronic medical conditions, including hypertension, dyslipidemia, coronary heart disease, diabetes mellitus, gallbladder disease, respiratory disease, some types of cancer, gout and arthritis. The majority of individuals who weigh more than 20% over their calculated ideal body weight (IBW) have excessive adipose mass. The body mass index (BMI), which is the ratio of weight (in kilograms) to height (in meters) squared (wt/ht^2), is the most convenient method of quantifying the degree of obesity. The National Center for Health Statistics has defined overweight as a BMI of 27.8 or more in men and 27.3 or more in women.

The critically ill obese patient presents the critical care team with many unique problems. Obesity increases the incidence of complications of patients admitted to an ICU, and it is likely that this is associated with a longer hospital stay and poorer outcome.

Significant abnormalities in lung function occur with obesity. The total lung capacity, functional residual capacity (FRC) and vital capacity are reduced by up to 30%. Lung function testing demonstrates a restrictive type of pattern. The work of breathing is increased. Patients with severe obesity are generally hypoxemic, with a widened alveolar-arterial oxygen gradient caused by ventilation-perfusion mismatching. Alveolar collapse and airway closure at the bases contribute to this phenomenon. The fall in FRC when assuming a supine position further increases ventilation-perfusion mismatching. This may result in severe arterial hypoxemia, and sudden death. The sleep apnea/obesity hypoventilation syndrome occurs in about 5% of morbidly obese individuals.

These alterations in pulmonary function have important implications in the management of the obese patients requiring mechanical ventilation. The small lung volumes and increased airway resistance necessitate the use of relatively small tidal volumes. The tidal volume should not be calculated according to the patient's weight, but rather determined by the airway pressures and blood gasses. The use of positive end-expiratory pressure (PEEP) may prevent end-expiratory airway closure and atelectasis, particularly in dorsal lung regions. In obese patients, neuromuscular paralysis affects respiratory mechanics and oxygenation more than in normal subjects. Intubated obese patients are more likely to develop atelectasis and ventilator associated pneumonia, which will prolong the duration of mechanical ventilation. Weaning the obese patient from mechanical ventilation is frequently a difficult task.

The risk of aspiration pneumonia is greatly increased in the obese patient. The risk of aspiration is increased due to several reasons including a higher volume of gastric fluid, a lower than normal pH of gastric fluid in fasting obese patients, increased intra-abdominal pressure and a higher incidence of gastroesophageal reflux.

Obese patients have been reported to have a higher incidence of postsurgical pulmonary complications. Postoperative pulmonary dysfunction is accentuated by thoracic and upper abdominal incisions. Preoperative spirometry is suggested in all obese patients undergoing elective surgery in order to predict the likelihood of postoperative respiratory complications. Pain control strategies with minimal respiratory depression, such as continuous epidural patient-controlled analgesia are recommenced. Postoperative respiratory monitoring with pulse oximetry, aggressive chest physiotherapy and early physical mobilization are recommended.

Obesity is the single most important risk factor for pulmonary embolism. Furthermore, obese patients have been documented to have a higher incidence of postoperative thromboembolic disease. Decreased mobility, venous stasis and an increased thrombotic potential may account for this finding. Diminished levels of antithrombin III and circulating fibrinolytic activity have

been demonstrated in obese patients. The high risk of thromboembolic disease in obese ICU patients warrants the use of both subcutaneous heparin and pneumatic compression for deep venous thrombosis prophylaxis.

Morbid obesity is characterized by an increase in total blood volume and resting cardiac output. The cardiac and stroke index are normal in obese patients. Baseline oxygen consumption is increased, with a normal arterio-venous oxygen difference, suggesting that the cardiac output increases primarily to serve the high metabolic requirements of excessive fat. Although the resting cardiac output is increased, obese patients have been demonstrated to have a depressed ejection fraction, both at rest and after exercise. Decreased myocardial β-adrenergic receptors may contribute to this finding. Furthermore, left ventricular mass, left ventricular wall thickness and left ventricular cavity size increase, resulting in left ventricular dilatation and hypertrophy. These changes are related to both the degree and duration of obesity. Systemic arterial hypertension is common in the morbidly obese patient, with superimposed left ventricular hypertrophy. Diastolic dysfunction with a prolonged relaxation phase and early filling abnormalities has been reported to be an early indicator of cardiac involvement in obesity.

The left ventricular filling pressure is elevated in obese patients due to the combination of increased preload and reduced ventricular distensibility. Consequently, fluid loading is poorly tolerated. As physical examinations are difficult and the signs of cardiac failure unreliable in obese patients, invasive hemodynamic monitoring may assist in titrating fluid therapy and assessing cardiac performance. Furthermore, as cuff sphygmomanometry can be inaccurate in the obese depending on the size of the cuff used, continuous monitoring of systemic blood pressure with an arterial cannula may be prudent in such patients.

Obesity alters the pharmacokinetics of various drugs depending on their physical and chemical properties and mode of metabolism. These factors must be taken into account when dosing obese patients. In many instances, toxic drug levels will be obtained if obese patients are dosed based on their actual body weight.

Although obese individuals have excess body fat stores and large lean body stores, they are likely to develop protein energy malnutrition in response to metabolic stress, particularly if their nutritional status was poor before injury. Nutrition should not be withheld from the obese patients in the mistaken belief that weight reduction is beneficial during critical illness.

Poor peripheral venous sites in obese patients necessitate more frequent use of central venous access. A short stubby neck, loss of physical landmarks and a greater skin-blood vessel distance make internal-jugular and subclavian vein cannulation technically difficult. This results in a higher incidence of catheter malpositions and local puncture complications. A greater number of skin punctures during catheter insertion and delayed catheter changes may lead to more catheter related infections and thromboses. Femoral venous access may not be possible as these patients usually have severe intertrigo. The use of doppler ultrasound-guided techniques for obtaining central venous access in high risk patients has been demonstrated to reduce the number of needle passes to cannulate the vein, with a reduction in the incidence of complications. Arterial line placement can also be challenging in these patients.

Therapeutic Hypothermia

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The use of therapeutic hypothermia (TH) over the past few years has increased worldwide. This technique has proven advantageous in a variety of clinical settings. TH lowers the cerebral metabolic rate in anoxic brain injuries and in cardiac arrest. TH has demonstrated a protective effect during cardiac and intracranial surgical procedures, where blood flow to the brain needs to be interrupted. TH has also been used during head-injured patients for the control of increased intracranial pressure that is refractory to hyperventilation, osmotherapy, ventricular drainage and barbiturates. In October 2002, the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation recommended TH in unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest when the initial rhythm was ventricular fibrillation. The Committee encouraged further research to expand the indications for therapeutic hypothermia to in-hospital cardiac arrests and perinatal

asphyxia. More recently, both the American Heart Association and The European Resuscitation Council have recommended therapeutic hypothermia for all comatose victims of cardiac arrest in which return of spontaneous circulation has been achieved.

Most investigators believe that hypothermia should be induced as early as possible. The earlier the TH is initiated, the earlier the target temperature was reached and the greater the chance of a positive outcome. The recommended duration for TH is from 12 to 24 hours according to International Liaison Committee on Resuscitation. In the study conducted by Bernard and coworkers, prolonged hypothermia (for 24 hours) demonstrated improvements in histologic outcomes compared with brief 4 hours therapeutic hypothermia. In the author's experience, patients experience best outcomes when TH is maintained between 48-72h.

There are several ways to induce TH. Among them, the most commonly utilized include surface cooling and invasive cooling. Surface cooling is relatively simple to use, but takes between 2 and 8 hours in reducing core body temperature. It can be accomplished by the use of ice packs, circulating cold-water blankets, cold air-forced blankets, alcohol baths and cold-water immersion. Among others, the most frequently used are the cold water blankets. Invasive cooling treatments include cold carotid infusions, single carotid artery perfusion with extracorporeal cooled blood, ice water nasal lavage, cardiopulmonary bypass, cold peritoneal lavage, nasogastric and rectal lavage, and the infusion of cold intravenous fluids (4°C). In infants, the selective induction of cerebral hypothermia by cooling the surface of the head and neck has proven to be beneficial. This method can be achieved with helmets or caps with circulating cold fluids. The infusion of cold intravenous fluids has been shown to be tolerable and feasible even in the prehospital setting. Bernard and coworkers infused large amounts (30 ml/kg) of Ringer's lactate at 4°C rapidly, without signs of pulmonary edema and with a significant decrease in the core temperature. Other methods to induce TH include devices, which require circulation of blood through an extracorporeal circuit, allowing for rapid infusion of cold fluids, oxygenation of blood during resuscitation and rapid delivery of intravenous drugs. Another type of endovascular cooling is an external heat exchange control device whose main objective is to circulate chilled saline to the indwelling venous that is placed percutaneously in the patient. Another method of active internal cooling is the hypothermic retrograde jugular vein flush, which has proven to be an alternative to achieve rapid brain cooling.

Rewarming after TH should be activated with the use of heating air blankets and allowing the core temperature to rise at 1°C per hour. During this time, shivering should continue to be suppressed as temperature increases. Intravenous fluid infusion may be helpful to maintain the mean arterial blood pressure as some patients may have sudden vasodilation upon rewarming.

Current recommendations with regards to use of TH include unconscious adult patients with spontaneous circulation after out-of-hospital cardiac arrest, near-drowning, anoxic brain injury, traumatic head injury, traumatic cardiac arrest, stroke, newborn hypoxic-ischemic encephalopathy, hepatic encephalopathy, bacterial meningitis, cardiac failure, postoperative tachycardia and the acute respiratory distress syndrome.

Several studies have reported complications particularly at lower temperatures (<32°C) and with uncontrolled maintenance of temperature. Among them dysrrhythmias, infections and primary coagulopathy are the most commonly noted. The Hypothermia After Cardiac Arrest (HACA) Study Group reported sepsis as the main TH complication; however, this did not reach statistical significance.

Research is now been directed towards establishing precise therapeutic window for benefit of patients in variety of clinical scenarios. In addition, the risk of complications with a variety of methods trying to obtain and control adequate temperature ranges for therapeutic purposes. Physicians are becoming more aware of the benefits of TH in the clinical settings and are beginning to incorporate it in their therapy. According to the HACA group, from the 375,000 people who suffer cardiac arrest in Europe each year, 30,000 would meet their inclusion criteria and TH could prevent an unfavorable outcome in 1,200 to 7,500 patients. It is essential for the health care providers to acknowledge the positive effect of TH patients and start implementing it as part of their therapeutic options.

Low Molecular Weight Heparin in DVT

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Intravenous (IV) infusion of unfractionated heparin (UFH) followed by oral administration of warfarin remains the cornerstone of clinical treatment of deep vein thrombosis (DVT). Results from numerous clinical trials demonstrate that subcutaneously administered low-molecular-weight heparin (LMWH) is at least as effective and as safe as IV UFH. Treatment with

LMWH has several clinical advantages over treatment with UFH, including less-frequent dosing and elimination of the need for monitoring.

LMWHs demonstrate reduced activation of platelets and a lower affinity for platelet factor 4 (PF4), which results in less neutralization of the anticoagulant effects of heparin. They do not increase microvascular permeability and are less likely to interfere with the interaction between platelets and vessel walls than UFH, resulting in lower incidences of bleeding. LMWH is cleared principally by the renal route, and the biologic half-life is increased in patients with renal failure.

Other advantages of LMWH include a longer half-life and better subcutaneous absorption. These characteristics result in LMWH producing consistent effects when given subcutaneously, allowing them to be administered without laboratory monitoring. The improved absorption, predictable response, and consistent effects of LMWH provide more rapid protection against PE than UFH, as they eliminate the concerns of subtherapeutic aPTT levels, frequent dosage adjustments, and intense monitoring.

LMWHs are fragments of commercial grade standard heparin produced by either chemical or enzymatic depolymerization. They have different mean molecular weights that vary from 4,000 to 6,500 daltons. LMWH inhibits thrombin generation by blocking the conversion of factor X to its activated form. The pharmacokinetic advantages of LMWH include (1) greater bioavailability; (2) dose-independent clearance; (3) decreased affinity for binding to plasma proteins and vascular endothelial cells; and (4) a higher anti-factor Xa to anti-factor Ua ratio (which ranges between two and four depending on the formulation). These advantages make the anticoagulant response of LMWH more predictable than UFH.

Commercially available LMWHs are made by different processes and differ both chemically and pharmacokinetically, which may result in differences in the anticoagulant effect. Each LMWH must be administered according to the recommendations specific to the particular preparation.

The introduction of LMWHs has made it possible for physicians to offer outpatient treatment of DVT, with the associated advantage of reduced costs due to shortened hospital stays. However, the optimal duration of anticoagulant therapy after DVT is still debated, as it depends on an individual patient's potential risk for recurrence or treatment-associated complications.

Patients are usually risk stratified on the basis of multiple clinical characteristics, including the location of thromboemboli, the presence or absence of cancer, the assumed etiology or cause of DVT (idiopathic vs. due to a transient risk factor), and the presence of certain thrombophilic conditions. High-risk patients often receive inpatient treatment with UFH or LMWH and are candidates for long-term (³6 months) oral anticoagulation, whereas short-term anticoagulation (3 to 6 months) is usually indicated for patients who are at lower risk of recurrence or therapeutic complications and who can be treated with LMWH on an outpatient basis. The introduction of LMWHs has resulted in significant clinical progress for the treatment of DVT.

TPN vs Enteral Feeding in the ICU

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Nutritional support is part of the standard of care for the critically ill adult patient. In the average patient in the intensive care unit who has no contraindications to enteral nutrition (EN) or parenteral nutrition (PN), the choice of route for nutritional support may be influenced by several factors.

EN is physiological and is superior to PN in terms of cost, decreased complications, ease of maintenance, efficacy of nutritional repletion, and maintenance of organ function. Providing even "token" EN diminishes gut mucosal atrophy and maintains gut integrity thereby preventing translocation of bacteria and toxins from the gut into the circulation. It is this translocation that results in the "stress syndrome". Early EN diminishes the cytokine production a key factor in multiorgan dysfunction.

There were 13 studies of Level II trials recently reviewed in a meta-analysis study (Nutrition. 2004; 20:843-848). The use of EN as opposed to PN was associated with a significant decrease in infectious complications (relative risk =0.64, 95% confidence interval =0.47 to 0.87, p =0.004) but not with any difference in mortality rate (relative risk =1.08, 95% confidence interval =0.70 to 1.65, p =0.7). There was no difference in the number of days on a ventilator or length of stay in the hospital between groups receiving EN or PN (Standardized Mean Difference [SMD] =0.07, 95% confidence interval =-0.2 to 0.33, p =0.6). PN was associated with a higher incidence of hyperglycemia. Data that compared days on a ventilator and the development of diarrhea

in patients who received EN versus PN were inconclusive. In the EN and PN groups, complications with enteral and parenteral access were seen. Four studies documented cost savings with EN as opposed to PN.

Conclusion:

The use of EN as opposed to PN results in an important decrease in the incidence of infectious complications in the critically ill and may be less costly. EN should be the first choice for nutritional support in the critically ill.

Optimizing Antibiotic Therapy in Patients with Severe Infection, Sepsis and Septic Shock

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Optimal antibiotic therapy starts with adequate initial therapy with approach to limit the emergence of antimicrobial resistance and good monitoring to the effect of the antimicroba.

Initial antibiotic therapy should be started promptly with optimal dose, to prevent excess hospital mortality of patients with serious infections. Initial antibiotic therapy should cover infecting pathogen(s), with adequate dose.

Approach to antibiotic administration to patients with severe infections can use de-escalating approach. The first step is hitting hard with initial appropriate therapy, without reserving broad-spectrum agents as a last resort. In seriously ill patients, we can start with a broad spectrum empiric agent such as carbapenem. Knowledge about local microbiological data is a big advantage as it can ensures that the correct pathogens will be covered. After initial therapy, the antibiotic administration then de-escalated according to clinical response and microbial susceptibility data. These data can be used as a guide to focused therapy and shorten the duration of therapy, or to stop therapy.

De-escalating approach can also limit the emergence of antimicrobial resistance. It can act as a potential strategy to limit antimicrobial resistance in the hospital setting by optimizing antimicrobial effectiveness and limit unnecessary antimicrobial utilization.

Patients who may have benefit from empirical broad-spectrum antimicrobial therapy are critically ill patients with serious infections such as patients with ventilator-associated pneumonia, nosocomial pneumonia, bloodstream infection, severe community-acquired pneumonia, and meningitis.