

**Extracorporeal Lung Support  
for  
H1N1 Disease  
in  
Alberta**

**Expert Working Group Recommendations**

**from**

**The Alberta Critical Care Network**

**July 20, 2009**

## Executive Summary

As the H1N1 pandemic spreads across the various continents more information becomes available on the impact this virus is having on critical care resources. Specifically, it is recognized that most of the affected people needing life supporting technologies are in the prime of their lives and most often do not have associated co-morbidities. The main challenge facing today's practitioners as evidenced by the ongoing experience in Manitoba and our colleagues in Australia and New Zealand is how to support young patients with single organ system failure (lungs) when conventional strategies are failing. Many of these patients have been placed on extra-corporeal membrane oxygenation (ECMO) with 50-60 % of patients who would have otherwise died surviving. The Alberta Critical Care Network structured a sub-committee of experts to review the current experience in both Canada and elsewhere in the world in using ECMO and less labor intensive technologies such as pumpless extra-corporeal lung assist devices (ECLA) for patients with catastrophic lung failure and more specifically in the context of an Influenza Pandemic and to make recommendations regarding the use of these technologies in our Province. The group was made up of physicians and nurses from Edmonton and Calgary. The recommendations were shared and subsequently endorsed by The Alberta Critical Care Network.

The recommendations are as follows:

- ECLS should be provided to select patients suffering from lung failure related to H1N1 disease failing all other support modalities. ECLS will be provided only as 'rescue' therapy.
- ECLS should be provided in a graded fashion being more restrictive as a pandemic limits the availability of resources. Three stages are identified:
  - Stage I      Early in pandemic with multiple patients on mechanical ventilation. Resource limitation likely in near future. No limitation to currently available ECLS resources.
  - Stage II     Some resource limitation to ECMO, either from lack of human resources, patient rooms, or a conscious decision to divert ECMO resources elsewhere to support critically ill patients.
  - Stage III    Severe resource limitation such that ECMO is not available.
- ECMO should be the preferred ECLS strategy to support failing oxygenation for as long as it is available.
- NovaLung technology should be established in Alberta to provide a less resource intensive alternative to ECMO when ECMO resources become limited or overwhelmed.
- NovaLung technology should be employed to initially support the minority of patients H1N1 related ARDS where the primary gas exchange problem is refractory hypercarbia.

# **Extracorporeal Lung Support in H1N1 Disease in Alberta**

## **Expert Working Group Recommendations**

**July 16, 2009**

### **Background**

Infection with H1N1 influenza can be associated with severe disease in a minority of patients. Most often, severe disease manifests as severe lung injury (ARDS) frequently requiring mechanical ventilation. It is increasingly recognized throughout the world that for a portion of patients, conventional and unconventional modalities of positive pressure ventilation are unable to support gas exchange in such patients. Given H1N1 disease disproportionately effects young otherwise healthy individuals, extracorporeal methods of life support (ECLS) are increasingly being considered and applied. ECLS comprises traditional extracorporeal membrane oxygenation (ECMO) delivered using a pump and newer pumpless technologies.

Given ECMO is already a limited resource in Alberta, and during a evolving influenza pandemic it would be expected to become a even more limited resource, it is important for clear criteria to be developed as to whether such resources will be offered and if so, with what criteria. In addition, alternative extracorporeal methods of gas exchange support should be explored for potential utility in the resource limited environment of a pandemic.

### **Mandate**

To review the technology, operational intricacies, clinical indications, efficacy, and cost of providing extracorporeal lung support (ECLS), via both pumped (ECMO) and pumpless modalities, in adult critically ill patients dying of lung failure in the setting of H1N1 disease. To make recommendations on the advisability of proceeding with the use of ECLS in patients suspected or proven of having H1N1 Influenza admitted with respiratory failure to any Alberta Intensive Care Unit

### **Membership**

Dr. Mohamed Zibdawi (co chair) – intensivist; medical director CVICU - UAH

Dr. Dan Zuege (co chair) – intensivist; medical director ICU - PLC

Dr. Paul Boucher – intensivist; medical director CVICU - FMC

Ms. Pam Hruska – clinical instructor – critical care - FMC

Dr. Calvin Lam – intensivist – CVICU and RGH

Dr. Bill Murtha – intensivist – RAH and UAH

Ms. Ellen Reil – clinical instructor – cardiovascular critical care - UAH

Dr. Gurmeet Singh – cardiovascular intensivist - UAH

## **Process**

1. Review of literature, existing ECLS recommendations and practice guidelines, and local experience
2. Survey of ECLS use and outcomes in other centres across Canada, UK and Germany for H1N1 disease
3. Review of alternative pumpless ECLS technologies
4. Consensus development of recommendations

## **Assumptions**

1. Scope to include adult patients with H1N1 disease leading to lung failure despite optimized positive pressure ventilation
2. Application of guidelines in the setting of a pandemic being imminent with initial time point of now where no critical care resource limitations exist
3. Expectation of increasing resource limitation over time as a pandemic progresses and need for graded approach to any ECLS use
4. Expectation that any resource limitation to ECLS will be equally applied to all disease processes potentially benefiting from ECLS (eg CV surgery)
5. The decisions of how and when to limit ECLS resources will be made at an executive AHS and/or provincial level

## **Ethics and basic principles**

Pandemic ethics imply a balance of patient triage, and redirection or restriction of resources to focus on areas of greatest need or greatest perceived benefit. Pump driven extra corporal support (ECMO) is an invasive therapy that requires a significant amount of resources. It is generally applied as a rescue therapy for patients who are failing other means and who would not likely survive without it. Patients with viral pneumonia have the best prognosis of all diagnoses for which ECMO has been applied (the Extracorporeal Life Support Organization (ELSO) database quotes a survival of 60% in such patients who would have likely died without it). Under non pandemic circumstances patients with influenza pneumonia that are failing mechanical ventilation would be considered for ECMO. Pumpless ECLS, while not currently in use in the province, requires significantly less use of resources but is clearly not as effective in supporting failing oxygenation. Whether it confers the same survival benefit is not known.

ECMO is a limited resource in Alberta. Currently up to 2 patients in Calgary and 3 in Edmonton could be treated at one time without impacting the cardiac surgical programs. Limiting the surgical programs to emergent cases only could see this number increase to 4 in Calgary and 5 in Edmonton. A pumpless system would not have the same implications but would still represent a finite resource based on the number of units available.

Patients generally require ECLS for a number of days (average of 12 days per ELSO database). This adds additional ethical dimensions in that patients may well be referred while patients are receiving the therapy who may be felt to have a better prognosis than those currently being treated. In addition, the availability of resources may change during a given patient's duration of ECLS therapy.

It is important to note that if the situation arises that ECMO will not be offered to patients with severe respiratory failure due to influenza pneumonia it would not be ethically sound to offer it to patients with other diagnoses with the same or worse expected outcomes. This especially given that patients with viral pneumonia have the best prognosis of all patients who are candidates for this therapy. This will have major implications for the cardiac surgical, heart and lung transplant, and heart failure programs in the province.

As ECMO has been used in the province historically to treat patients with severe respiratory failure and is being used in other tertiary care centers in Canada currently for patients with H1N1, it is difficult to initially refuse to offer this modality to patients until a severe restriction on services is required given lack of resources or redirection of such resources to other areas. Pumpless ECLS has been offered to H1N1 patients in other centers in Canada but is not currently available in Alberta. Other centers have brought in this technology and have applied it to patients in less than 72 hours.

Given the magnitude and length of time such resource utilization can be expected to be required in the setting of constantly changing demands that a pandemic would place, a graded approach to the use of ECLS is warranted. Restrictive inclusion criteria should be applied in the early stages of a pandemic focusing on patients with the best perceived prognosis. As demand for ECLS increases and/or the amount of available ECLS resources decreases, more restrictive entry and exit criteria will need to be applied eventually culminating in a stage where ECLS would not be offered at all. Given the differences in resources required, it is expected that ECMO will be limited at an earlier stage and to a greater extent relative to less resource-intensive pumpless technologies.

### **Survey of other centres ECLS use in H1N1 disease**

A brief survey was conducted among major referral centres across Canada and select centres in other countries. Email, list-serve and phone methods of contact were used. Listed below are all responses received:

Winnipeg – ECLS has been offered to patients suffering from H1N1 disease who are otherwise well and suffering from single system failure. 3 patients have been supported with ECMO thus far. One patient failed prior use of a NovaLung.

Halifax – ECLS is offered. 2 patients have been supported – one with ECMO and one with a NovaLung.

Toronto – ECLS is offered. One infant with H1N1 disease has been supported with ECMO.

Vancouver – no patients have deteriorated to point of considering ECLS. They are considering criteria

London, Ontario – no patients have deteriorated to point of considering ECLS. They are considering criteria

Ann Arbor, Michigan – ECLS referral centre. H1N1 disease is being supported. 9 patients with H1N1 disease supported thus far, all with ECMO. 50% survival so far.

## **Current Alberta ECLS resources**

Currently, ECLS in Alberta exists only as ECMO. Pumpless ECLS technologies are currently not available in Alberta. ECMO is available only at UAH and FMC and is usually provided within the CVICU's of those centres. ECMO requires machines, access catheters, perfusionists, and critical care nurses and physicians with ECMO expertise. Though ECMO is usually provided with dedicated ECMO machines, it can also be provided using cardiopulmonary bypass machines normally used for CV surgery.

FMC – Currently able to support 2 patients on ECMO with continued operation of CV surgery program. Able to support up to 4 patients on ECMO with conversion of CV surgery program to emergent surgery only. In the setting of H1N1 disease, management of one patient in the one single patient room in CVICU; use of 4 bed single room (CICU) to cohort patients with confirmed H1N1 disease when >1 patient is supported with ECMO. Potential for one perfusionist to supervise multiple patients if cohorted.

UAH – currently able to support 3 patients on ECMO with continued operation of CV surgery program. Able to support up to 5 patients on ECMO with conversion of CV surgery program to emergent surgery only. In the setting of H1N1 disease, management of two patients in the two single patient rooms in CVICU; use of additional single patient rooms in the general systems ICU to manage patients when >2 patients are supported. Potential for one perfusionist to supervise multiple patients if cohorted.

## **Recommendations**

### **Overall ECLS strategy**

1. ECLS should be provided to select patients suffering from lung failure related to H1N1 disease failing all other support modalities. ECLS will be provided only as 'rescue' therapy.
2. All other available support modalities should be tried before considering ECLS. These modalities should include all available conventional and unconventional modalities of positive pressure ventilation and use of adjunctive positioning and pharmacologic measures to improve gas exchange.
3. ECLS should be provided in a graded fashion being more restrictive as a pandemic limits the availability of resources. Three stages are identified:

Stage I	Early in pandemic with multiple patients on mechanical ventilation. Resource limitation likely in near future. No limitation to currently available ECLS resources.
Stage II	Some resource limitation to ECMO, either from lack of human resources, patient rooms, or a conscious decision to divert ECMO resources elsewhere to support critically ill patients.
Stage III	Severe resource limitation such that ECMO is not available.

Currently in Alberta we are in Stage I of this schema where currently available ECLS resources are not yet limited or overwhelmed.

4. ECMO should be the preferred ECLS strategy to support failing oxygenation for as long as it is available.
5. NovaLung technology should be established in Alberta to provide a less resource intensive alternative to ECMO when ECMO resources become limited or overwhelmed.
6. NovaLung technology should be employed to initially support the minority of patients H1N1 related ARDS where the primary gas exchange problem is refractory hypercarbia.
7. NovaLung technology should be additionally used to support failing oxygenation when ECMO resources become more limited or non-existent.
8. ECLS must only be provided in strict abeyance of all infection control practices related to H1N1 disease (eg only in single patient rooms or cohorted areas where multiple patients with H1N1 can be managed in the same enclosed space). ECLS will not be provided in open patient areas where non-H1N1 patients are managed.

The suggested overall strategy to the provision of ECLS to patients with H1N1-associated lung failure is illustrated in **appendix 1**. The suggested phased entry and exit criteria for the provision of ECLS according to this algorithm are listed in **appendix 2**.

### **Pumped ECLS (ECMO)**

1. ECMO should continue to be offered, as per current established practice, as rescue therapy to select patients suffering from failing gas exchange despite other measures for as long as it is available in the setting of a pandemic.
2. ECMO is the preferred ECLS strategy to support failing oxygenation. NovaLung technology provides an alternative therapy to the minority of patients with H1N1 related ARDS where the primary gas exchange problem is refractory hypercarbia.
3. In the setting of an imminent pandemic, ECMO should be provided in a graded fashion being more restrictive as a pandemic limits the availability of resources (see **appendix 2**). There is the recognition and expectation that as a pandemic progresses and the number of critically ill patients with respiratory failure increases and human and physical resources become limited, that ECMO will be increasingly restricted and eventually not offered.
4. Though ECMO resources (equipment and perfusionists) may be moved between Calgary and Edmonton, for safety and logistical reasons, patients will not be moved between Calgary and Edmonton.
5. ECMO will continue to be only offered in the FMC CVICU/CICU and UAH CVICU and GSICU. For patients at other hospitals unable to be safely transported with

positive pressure ventilation, ECMO will be initiated at the site with transfer following.

6. As ECMO resources become more restricted, more rapid and aggressive ECMO weaning strategies should be employed to enhance its availability (see **appendix 2**).

**Appendix 3** provides an overview of ECMO as currently applied in Alberta.

### **Pumpless ECLS (NovaLung)**

1. NovaLung is the only feasible pumpless ECLS technology available.
2. NovaLung technology should be made available in Alberta to minimize the use of ECMO resources and to use as an alternative to ECMO when ECMO becomes unavailable. The key arguments in favor of its use are:
  - a. Feasibility and ease of use relative to ECMO;
  - b. Significantly less human and financial resources required to use relative to ECMO;
  - c. Can be initiated and provided any of the urban ICU's in Alberta avoiding need for patient transfer;
  - d. Can be used for prolonged periods of time (weeks).
  - e. Less need for blood products relative to ECMO
  - f. Use as a stepdown therapy for patients on ECMO allowing for minimization or diversion of limited ECMO resources to other patients
  - g. Successful use elsewhere in general and specifically with this disease process;
  - h. Its use with this disease process has been introduced in several other jurisdictions.
3. NovaLung should be applied in an ECLS algorithm in a staged manner, being used initially for patients with refractory hypercarbia and increasingly for failing oxygenation as ECMO resources become limited in availability.
4. The entry criteria for Novalung should be identical to that for ECMO (see **appendix 2**)

**Appendix 4** provides a more detailed overview of NovaLung technology including a summary of the available literature, indications, contraindications, advantages, disadvantages and cost estimates.

## **Suggested Next Steps**

1. Review and endorsement of this guideline by:
  - Calgary and Edmonton critical care leadership
  - Critical Care leadership outside of Calgary and Edmonton
  - Cardiac sciences, CV surgery and CV anesthesia divisions in Edmonton and Calgary
  - Provincial pandemic committee(s)

Accountable: Drs. Noel Gibney and Paul Boiteau

2. Development of an algorithm for early transfer of failing patients with H1N1 disease in ICU's outside of Calgary and Edmonton to allow access to advanced ventilatory modalities, adjunctive gas exchange measures, and potentially ECLS.

Accountable: Drs. Mohamed Zibdawi and Calvin Lam

3. Adoption and establishment of NovaLung technology in Alberta:
  - Create detailed provincial use guideline (modification of manufacturer's documentation) targeting ECLS support team members
  - Create less detailed provincial use guideline (modification of manufacturer's documentation) targeting bedside users
  - Create learning module(s) for bedside users (examples available in other centres)
  - Adopt existing ECLS teams in Calgary and Edmonton to support initiation and initial supervision of NovaLung technology
  - Detailed training of ECLS team staff by NovaLung
  - Purchase of 8 NovaLung units (4 initially based in each city with transfer to meet needs) with associated vascular access cannulae to support initial Alberta needs
  - Consideration should be given to the development of and participation in a national strategy for NovaLung purchase

**Appendix 5** contains a more detailed description of suggested ECLS support and educational needs.

Accountable:

Drs. Mohamed Zibdawi and Calvin Lam/Paul Boucher, Ms. Ellen Reil and Pam Hruska, Dr. Cheri Nijssen-Jordan and Nancy Guebert

4. Dissemination of finalized CPG to all critical care providers in Alberta

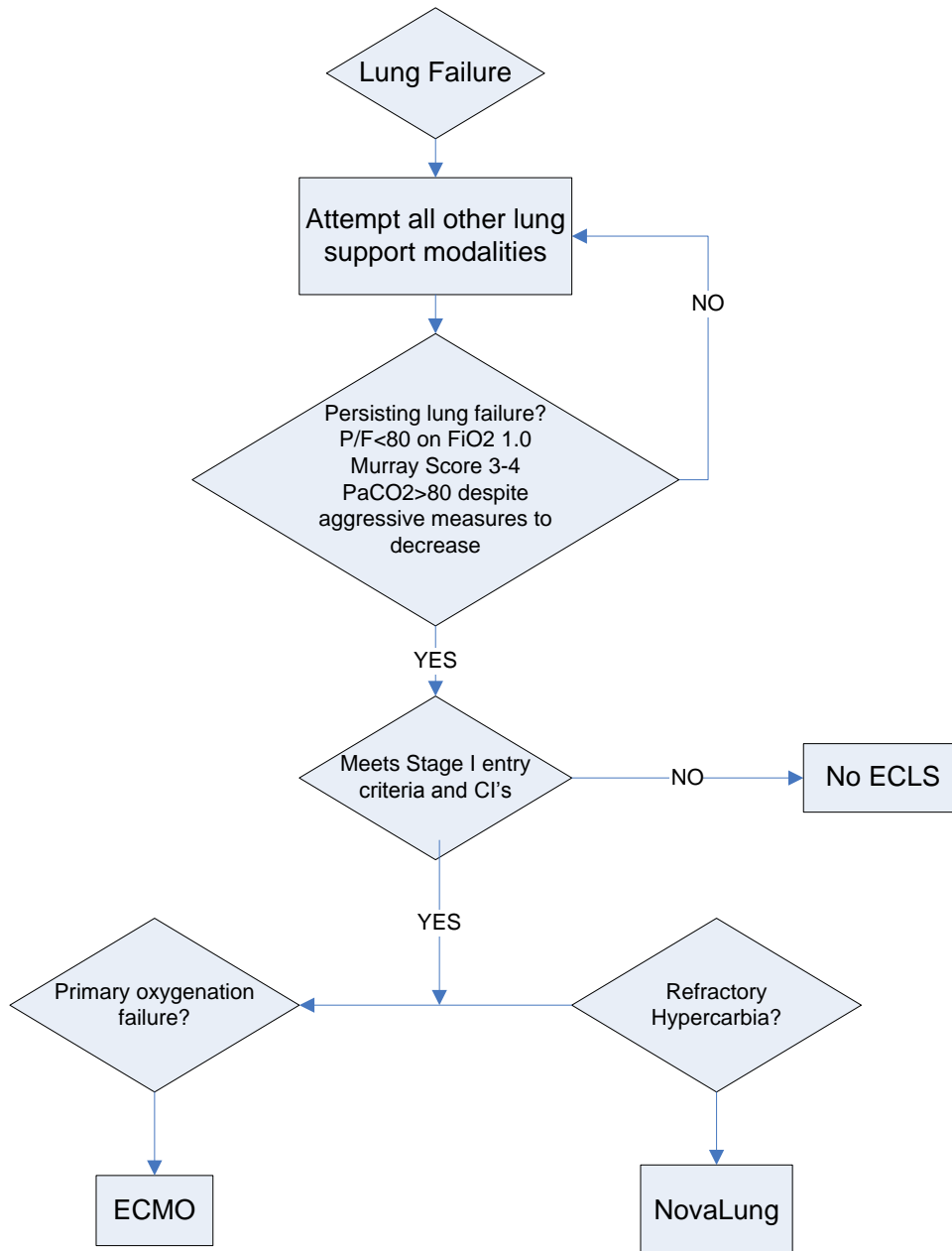
Accountable:

Drs. Noel Gibney and Paul Boiteau vi the Alberta Critical Care Network

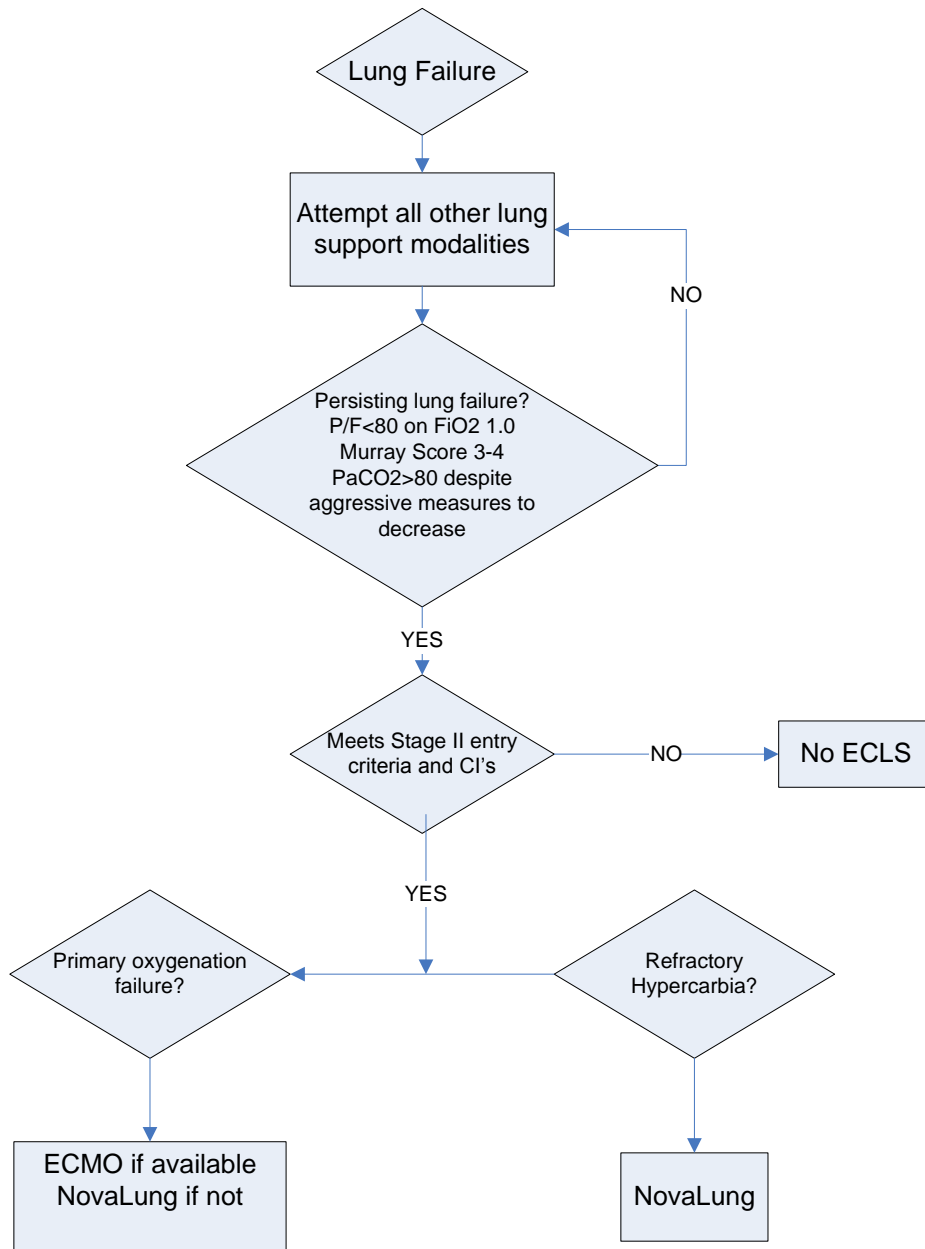
## Appendix 1

### ECLS Strategy for H1N1-associated Lung Failure

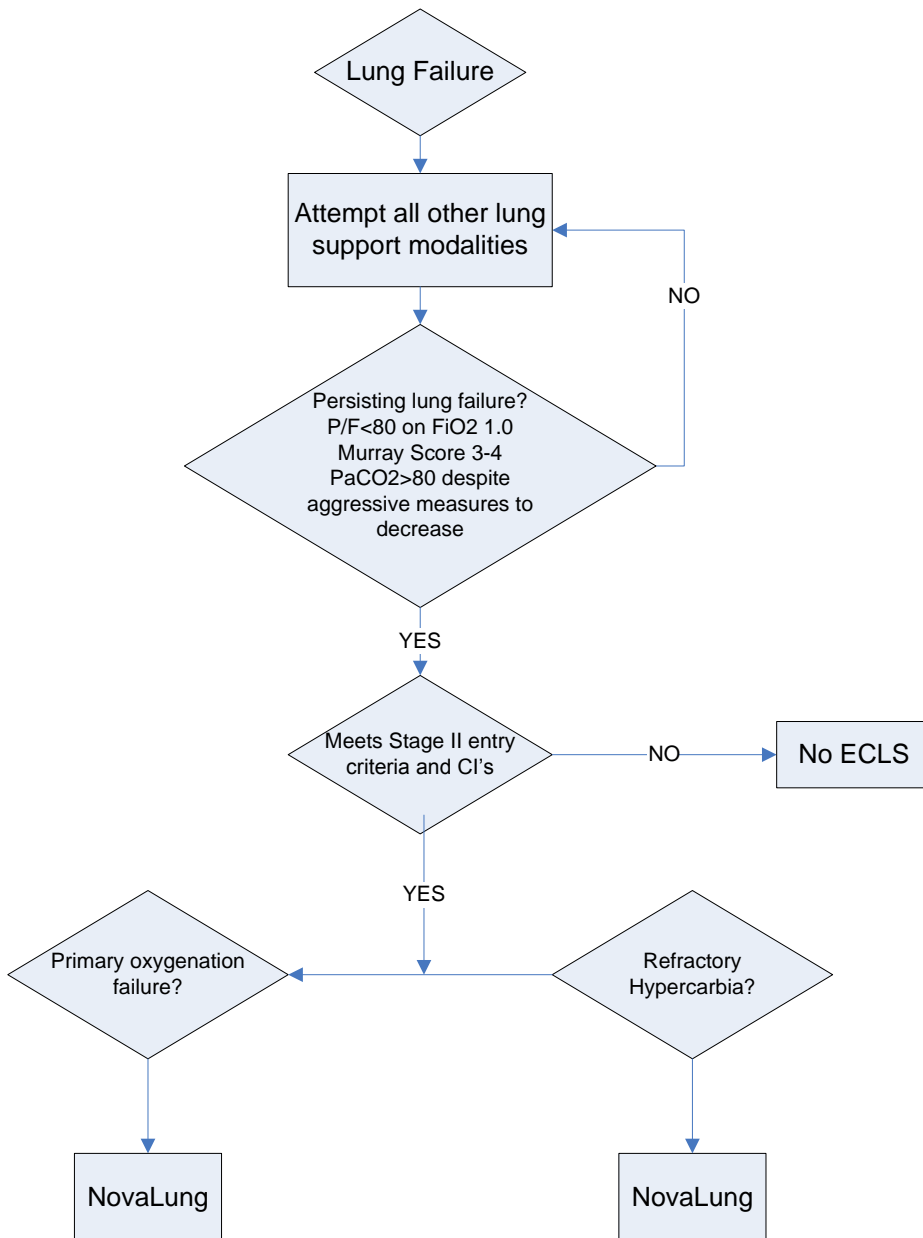
#### ECLS Strategy H1N1 disease Stage I



## ECLS Strategy H1N1 disease Stage II



# ECLS Strategy H1N1 disease Stage III



## Appendix 2

### **Selection Criteria for ECLS in Patients with H1N1-associated Lung Failure**

Extracorporeal Life Support (ECLS) is indicated for patients with H1N1-associated pneumonia when they develop respiratory failure severe enough that their predicted mortality exceeds 80%. ECMO may allow for 50-60% survival in patients with viral pneumonia.

These criteria have been adapted from the recently published guidelines put forth by the Extracorporeal Life Support Organization (ELSO) in April 2009. The criteria presented here-in are necessarily more restrictive than the ELSO Guidelines due to the current limitation in ECLS resources in Alberta and the potential large number of patients which may require these resources during a pandemic. It is expected that any resource limitation to ECLS will be equally applied to all disease processes potentially benefiting from ECLS (eg CV surgery).

The selection criteria for H1N1 pneumonia patients to receive ECLS will be restricted in a graded fashion, with greater limitations applied as the demand for ECLS outstrips the amount of available ECLS resources and/or the amount of ECLS resources decrease as a pandemic progresses. These restrictions are driven by clinical factors which are known to affect patient prognosis and outcome. The goal is to use the limited ECLS resources on patients with the greatest likelihood of survival. The application of ECLS entry criteria should be equally applied to all patients referred for the same resource.

Mechanical ventilation (MV) will remain the primary therapy for patients with H1N1 pneumonia. ECLS will only be considered if the patient fails optimized MV support. Optimized MV support should include at a minimum, where available, all of the following:

1. Advanced ventilator modes including inverse ratio pressure control ventilation (IR-PCV) and airway pressure release ventilation (APRV);
2. Aggressive titration to high levels of positive end expiratory pressures (PEEP);
3. Adequate sedation and pharmacologic paralysis;
4. Control of fluid status (limitation of intake; aggressive diuresis);
5. Prone positioning;
6. Inhaled nitric oxide (NO) and/or inhaled epoprostenol;
7. High frequency oscillatory ventilation (HFOV); and
8. Adequate time to determine effects of above.

If the patient remains in life-threatening respiratory failure despite these maneuvers then ECLS can be considered.

All patients referred for consideration of ECLS in the setting of H1N1-associated disease will have application of these guidelines. In addition, discussion will always ensue with the local ECLS support team where each case will be assessed and consensus decision making applied. Such decision making should always be in abeyance with these guidelines for minimal entry criteria.

## **Stage I - No limitation to currently available ECLS resources**

Veno-venous ECMO will be the primary modality of ECLS to support failure of oxygenation in this stage. The NovaLung will be considered as initial ECLS therapy for the small minority of patients with ARDS with refractory hypercarbia yet relatively preserved oxygenation.

### **A. Indications**

1. Hypoxemic respiratory failure
  - PaO<sub>2</sub>/FiO<sub>2</sub> < 80 on 100% O<sub>2</sub>
  - Murray Score 3-4
2. Hypercapneic respiratory failure
  - PaCO<sub>2</sub> > 80 despite aggressive measures to control hypercarbia
3. The above despite aggressive attempts at optimal MV support as described above

### **B. Contraindications**

1. MV at high settings (FiO<sub>2</sub> > 90%, Pplat > 30 cm H<sub>2</sub>O) for 7 days or more
2. Contraindication to systemic anticoagulation
3. Age > 60 years
4. Morbid obesity (BMI>40)
5. Cachexia/severe malnutrition
6. Co-morbidities which will have significant impact on short or medium term outcomes or present technical difficulties to the delivery of ECLS. Examples include but are not limited to:
  - severe lung disease with home oxygen requirement, chronic hypercapnea, or pulmonary hypertension
  - Class IV cardiac disease
  - Liver disease with portal hypertension, previous variceal bleeds, or hepatic encephalopathy
  - chronic renal failure requiring dialysis
  - severe peripheral vascular disease
  - long standing diabetes mellitus with end organ damage
7. Metastatic or otherwise advanced malignancy
8. Immunosuppression
  - pharmacologic suppression with absolute neutrophil count <400/ml<sup>3</sup>
  - acquired immune deficiency syndrome

9. Low pre-morbid functional status/high dependant state. Examples include but are not limited to:
  - chronic dementing illness
  - patients from chronic care facilities/nursing homes
  - patients unable to independently perform ADLs
10. Necrotizing pneumonia
11. Refractory septic shock
12. Multisystem Organ Failure
  - this does not preclude the presence of some degree of organ dysfunction particularly if the organ dysfunction is minor and related to the therapy for the H1N1 pneumonia. For example, mild renal dysfunction felt to be pre-renal associated with diuresis to assist lung function on MV.
13. Moribund/not expected to survive >7 days from non-pulmonary disease states

**C. Exit Strategy**

Per existing practices of weaning from ECMO

**Stage II – Some limitation to currently available ECMO resources**

Veno-venous ECMO will continue to be the primary modality of ECLS to support failure of oxygenation in this stage as much as it is available and with increasingly restrictive access criteria. The NovaLung will continue to be considered as initial ECLS therapy for the small minority of patients with ARDS with refractory hypercarbia yet relatively preserved oxygenation. The NovaLung will now be considered for patients with oxygenation failure when ECMO resources cannot meet the demand.

**A. Indications**

1. All of the indications from Stage I
2. ECLS resources will be reserved for patients with viral pneumonia or conditions with a similar or better outcome. No other use will be allowed.

**B. Contraindications**

1. All of the contraindications in Stage I in addition to:
  - Age > 40 years
  - evidence of any organ dysfunction other than pulmonary

### **C. Exit Strategy**

In order to free up ECMO resources for use in other more suitable patients, ECMO may be terminated in a particular patient if the patient has improved enough to return to MV or if they are deteriorating despite therapy. Termination of ECMO will be considered in the following situations:

1. Improvement in pulmonary function that patient can be sustained on optimized MV. This may or may not include the adjunctive use of a NovaLung device.
2. Development of ventilator associated pneumonia, non-pulmonary sepsis, or multisystem organ failure
3. Development of pulmonary emboli
4. Bleeding complications
5. No significant improvement in pulmonary function after 14 days of ECMO.

### **Stage III - No ECMO resources are available**

Optimized mechanical ventilation will be the mainstay of therapy. The NovaLung will be the only available ECLS therapy to support patients with either oxygenation failure and/or refractory hypercarbia.

#### **A. Indications**

Identical to that in Stage II

#### **B. Contraindications**

Identical to that in Stage II

#### **C. Exit Strategy**

Identical to that in Stage II

## Appendix 3

### ECMO Overview

Historically, extracorporeal support has been offered to select patients in both Edmonton and Calgary with severe oxygenation and/or ventilation failure. Veno-venous ECMO (pump driven ECLS) is used in both centers as rescue therapy for severe respiratory failure in patients that are felt to have a reasonable chance of survival. In the last few years at least one patient with H1N1-associated respiratory failure has been successfully supported with ECMO in Calgary.

Venovenous ECMO is a pump driven oxygenation system that involves oxygenating blood in an extracorporeal fashion via a membrane oxygenator. Two venous cannulae are inserted into central veins by a cardiac surgeon. The technology and team are generally initially taken to the patient as they are often too unstable to transport. The patient is cannulated and ECMO is initiated and continued during transport to the CVICU. Due to the need for perfusionist support, these patients must be cared for in the same center as the adult cardiac surgical programs (FMC and UAH CVICU's). These patients generally require 1 to 1 nursing. The model in both Edmonton and Calgary is to have a perfusionist at the bedside continuously. Different models exist in other centers in Canada and internationally that use an 'on-call' system for perfusionist support. It is conceivable if a perfusionist is required on site that they could provide support to multiple patients. These patients still require a ventilator but not advanced ventilatory techniques and often require blood products to manage bleeding.

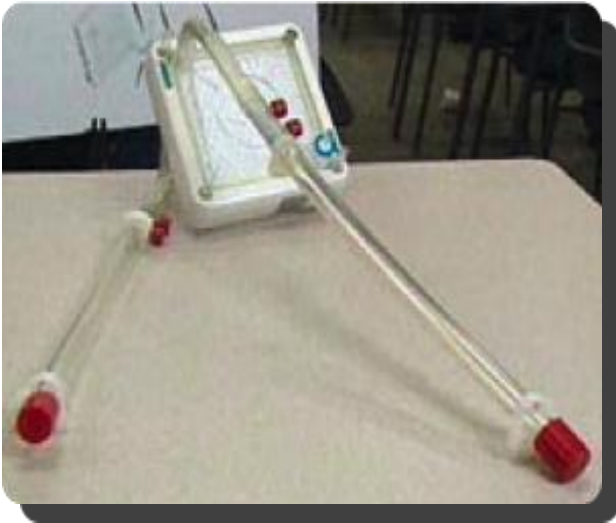
## Appendix 4

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# Extracorporeal Ventilation

NOVALUNG® iLA MEMBRANE VENTILATOR™ THERAPY

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Novalung® iLA Membrane Ventilator™

## **Background**

Extracorporeal Life Support (ECLS), in particular ECMO, has been used for cardiopulmonary support in an effort to permit organ recovery or bridge to transplantation. ECLS circuits are typically pump driven.

Recently, an extracorporeal ventilatory system that is not pump-dependent has been introduced. The iLA (interventional Lung Assist), developed by Novalung GmbH (Germany), distributed in Canada by CARE stream Medical, Inc., is an extracorporeal diffusion membrane gas exchange device. The system is entirely heparin-coated. Blood flows outside a plasma-proof membrane, while oxygen gas flows inside the membrane. The gas flow (sweep) determines the degree of CO<sub>2</sub> removal, while blood flow determines the degree of improvement in PO<sub>2</sub>.

This extracorporeal gas exchange membrane is marketed by the company as an “extra pulmonary ventilation system.” (iLA Membrane Ventilator™, Novalung Product Info. PDF, from [www.novalung.com](http://www.novalung.com)). The main function of the membrane is CO<sub>2</sub> elimination via a heparin-coated diffusion membrane, connected to the patient via arterial and venous femoral cannulae. The system is approved for use up to 29 days.

The femoral artery is cannulated, and serves as inflow to the membrane. The patient’s native blood pressure and cardiac output is used to drive blood flow. The femoral vein is cannulated as outflow from the iLA membrane, for blood to be returned to the patient.

Conceptually, extracorporeal ventilation is an attractive method to improve CO<sub>2</sub> clearance, and may ultimately permit greater compliance with lung protective ventilation strategies. Improvements in oxygenation have been observed but appear to be more modest.

## **Literature Summary**

The available literature suggests iLA has the ability to successfully augment support of patients refractory to conventional and advanced modes of mechanical ventilation. The largest experience currently comes from Europe.

Most reports describe support for ARDS. However, at least one group has successfully treated viral (varicella) pneumonia with Novalung support [von Mach MA, Kaes J, Omogbehin B, Sagoschen I, et al. *Lung* 2006;184(3):169-75].

iLA is used in conjunction with mechanical ventilation and has been used with both high-frequency oscillatory ventilation as well as conventional modes. With iLA support,

centres have observed improvement in oxygenation (eg. PaO<sub>2</sub>/FiO<sub>2</sub> ratios improving from 50 to 110 mmHg -Liebold A, Phillipp A, Kaiser J, Merk F-X, et al. *Minerva Anestesiol* 2002; 68:387-91). The latest report from the same centre (Bein T, Weber F, Phillip A, Prasser C, et al. *Crit Care Med* 2006; 34:1372-77) of Novalung® iLA Membrane Ventilator™ usage described 90 patients with respiratory failure supported with iLA for a mean duration of 5±5 days. The average PaO<sub>2</sub>/FiO<sub>2</sub> ratio improved from 58 to 101 within 24 hours, and mean PCO<sub>2</sub> dropped from 60 to 34 mmHg. The iLA flows were 2.2 L/min, with patient cardiac outputs between 9 and 10 L/min (eg diverting approximately 20-25% of cardiac output). The manufacturer of Novalung reports an average 17% increase in PaO<sub>2</sub> with iLA therapy.

### **Canadian Data**

The Canadian experience with iLA is currently small but rapidly growing. Toronto General Hospital has experience in running 14 patients thus far on the NovaLung, some of these patients being bridged to lung transplant. With respect to novel influenza A (H1N1), the iLA has been used in Winnipeg to support a 14 year old patient for 16 days who has subsequently been transitioned to conventional mechanical ventilation. In Halifax, the experience in a pandemic setting has suggested some utility of the iLA for improving oxygenation.

### **Indications**

The primary marketed indication for this device is to aid in the management of marked respiratory acidosis due to primary hypercapnic respiratory failure. The company lists the following potential indications:

1. Acute lung injury/ARDS
2. Prolonged weaning from mechanical ventilation
3. Acute exacerbation of COPD
4. Bridge to transplant
5. Post-transplant/tracheal surgery support
6. Critical care transport

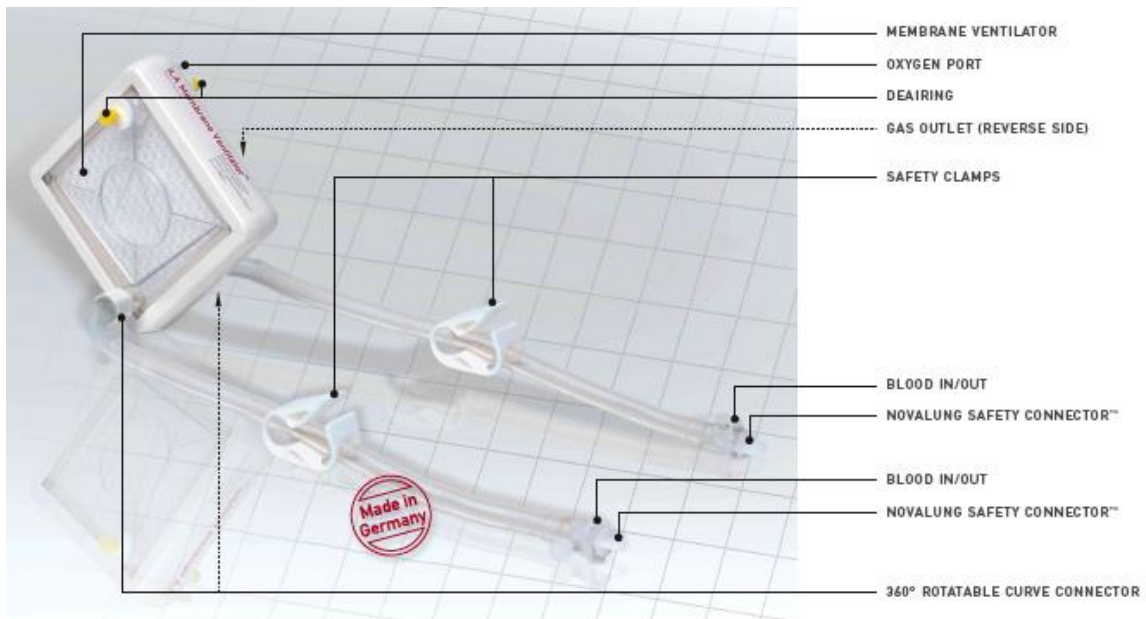
**Marketed contraindications** include:

1. HIT
2. Septic Shock
3. Cardiogenic Shock
4. Peripheral vascular disease (affecting the femoral artery)
5. Patient weight < 20 kg

### Complications

Potential complications include bleeding, infection, limb ischemia and clotting of the membrane. United States military usage confirms the potential for limb ischemia complications related to the arterial cannulae in young, previously healthy, trauma victims (Personal Communications).

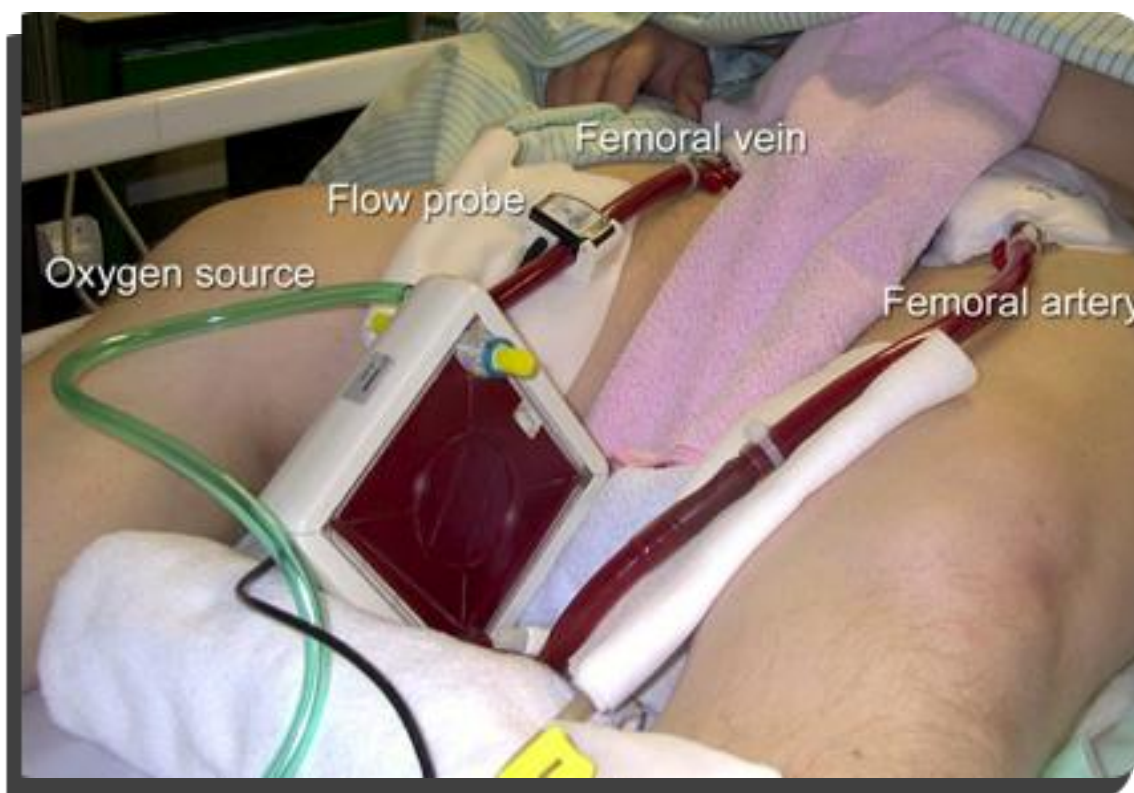
### Technical



Technical Data	
Blood flow rate	0.5–4.5 L/min
Gas exchange area	1.3 m <sup>2</sup>
Max. Gas flow	10 L/min
Filling volume	240 ml
Pressure limit MAP	350 mmHg
Gas inlet and outlet	1/4"
Connection to cannulae	Novalung Safety Connector
Deairing port with bacterial filter	

Technical Data	
Recommended ACT	120 - 140 seconds
Typical Blood Flow	0.5 - 2.5 L/min
Priming Volume (NS)	240 mL

### Cannulation



Femoral arterial and venous cannulation is required. Cannulae are purchased separately from the iLA membrane. Apparently, proprietary cannula usage is mandatory. Both arterial and venous cannulations are performed by a percutaneous approach, using the Seldinger technique, by either intensivists or cardiac surgeons. Cannulation is performed at the bedside at the patient's current location of care. A blood flow meter is placed on the outflow limb of the circuit, downstream from the iLA membrane. Suitable blood flow meters are already in use in both Calgary and Edmonton. Low dose heparin is infused in inflow limb of the circuit aiming for a PTT of 55-60 (ACT 150). Current recommendations for arterial cannula placement include preparatory ultrasound to measure size of the femoral artery. An arterial cannula approximately one-half the size of the vessel is then selected. Such vascular ultrasonography is now common place in Alberta tertiary ICU's.

**Cost**

iLA Membrane Ventilator	\$5000.00
Arterial cannula	\$735.00
Venous cannula	\$735.00
Flow monitor *	no cost
<b>Totals</b>	<b>\$6470</b>

\* Flow monitors are already part of currently existing ECMO systems at Foothills Medical Centre, Calgary and Mazankowski Alberta Heart Institute/Stollery Children's Hospital, University of Alberta, Edmonton

## Summary

The Novalung® iLA Membrane Ventilator™ is a non-pump driven extracorporeal ventilatory system. The key advantages of the circuit include:

1. No pump requirement;
2. No ongoing perfusionist presence at the bedside required;
3. Peripheral percutaneous insertion at the bedside with ongoing patient care in any of the urban ICU's in Calgary or Edmonton;
4. Ease of insertion - an appropriately-trained non-surgeon could cannulate;
5. Has been used to transport critically ill patients;
6. Inexpensive, when compared to the overall acquisition and operational costs of running ECMO;
7. Improved CO<sub>2</sub> clearance
8. Indications of some improvement in oxygenation, making this a viable alternative to ECMO when such resources are limited or unavailable

Disadvantages of this system include limited experience in Canada and the fact that its primary physiologic benefit is CO<sub>2</sub> removal. Oxygenation improvements have been demonstrated but appear to be more modest. Because the function of the circuit is dependent on the patient's native blood pressure and cardiac output, one can reasonably expect greater gains in oxygenation with this technology in a younger population (such as the expected demographic of those suffering from H1N1-associated disease and in particular the age set proposed in the ECLS algorithm in appendices 1 and 2).

Finer control of CO<sub>2</sub> may permit "ultraprotective" lung ventilation strategies with tidal volumes as low as 3 mL/kg. It is unclear whether this will improve mortality, but it is possible that even lower tidal volumes may attenuate ventilator induced lung injury.

During a pandemic, if patients are supportable with iLA as opposed to ECMO, it will free up perfusionist personnel. It is also expected that blood product transfusion requirements with iLA would be significantly less relative to ECMO.

We also envision that the iLA may be a suitable “step-down” device for patients already being supported with ECMO, allowing ECMO resources to either be minimized and/or freed up for other patients.

Finally, this device appears to have sustainability once placed. iLA membranes may be left in place for up to 29 days. Prolonged iLA support has been used in Winnipeg for a H1N1 patient. The median duration of support from European centres has been 4 to 6 days with a large range (up to 35 days).

### **Recommendations**

Given that the Novalung is much better at reducing CO<sub>2</sub> levels than increasing oxygenation, it should be initially used primarily for patients with refractory, severe hypercapnea. If pump driven ECLS (ECMO) is still available as a support modality for patients, it is the preferred modality for supporting primary oxygenation failure (Stage 1). As demands on resources and ECMO increase, the role of the Novalung should be expanded. Under these circumstances (Stage 2) it could be used for patients with primary oxygenation failure as a means to spare the more limited ECMO resource or even as a triage modality such that only patients that fail Novalung would be transitioned to ECMO. Once ECMO is no longer available (Stage 3) pumpless systems would be used as the primary rescue therapy for patients who have no other options.

## Appendix 5

### ECLS teams/Educational Considerations with ECLS in Critical Care

#### **ECLS Teams**

ECLS is currently supported in Alberta by teams in Calgary and Edmonton. These teams consist of intensivists with ECMO expertise, CV surgeons, perfusionists and ECLS/VAD support nurses. These teams are currently able to initiate ECMO remotely and transport/help support patients on ECMO in the CVICU's in Calgary and Edmonton. They are available 24/7 through an on-call system.

It is proposed that NovaLung technology could be adopted via the existing human resources of ECLS teams. ECLS teams would be responsible for the initial assessment for ECLS (ECMO or Novalung) and the initiation and initial (hours) supervision of Novalung therapy. Further care for Novalung patients would be provided by the bedside nursing, respiratory, and intensivist resources at the local site. ECLS team members would be available for advice 24/7. In addition, representatives of the Novalung company are available 24/7 for technical assistance via phone.

#### **Educational Needs of ICU Staff**

Recommendations for the introduction of the NovaLung from an educational perspective would focus on capturing multidisciplinary staff members caring for ECLA patients. Targeted staff would include RRTs, RNs, and intensivists. Core groups to go through initial training would include all clinical nurse educators, RN clinicians, prn charge nursing staff, RRT educators, RRT clinicians and prn charge RRT staff, intensivists and critical care residents/fellows.

NovaLung sales representatives inform us that all educational materials and supports required for the introduction and support of this device are available at this time. Previously, if needed, the company has demonstrated the ability to personally provide bedside training for initial patients placed on the NovaLung within 72 hours. This training was provided by the clinical specialist at the bedside, and therefore only addressed the need for rapid initiation of treatment and would not inform large numbers of staff.

A clinical specialist with NovaLung would be the initial trainer for staff, and a 'train the trainer' approach would work best so that in house training would be offered after

introduction to this technology. A relationship with the clinical nurse educator in MSICU Toronto General Hospital has also been established, availing us collaboration with a centre that has experience in running 14 patients thus far on the NovaLung.

Educational delivery methods would include a didactic session with hands on exposure, as well as access to online reference materials. After initial training sessions, educators would have a pivotal role to capture the remaining staff. A 3-4 week offering of repetitive learning sessions on NovaLung should be offered so that a goal of 70% of all critical care staff are prepared to care for NovaLung patients. This would be of importance to avoid future challenges related to staff assignment allocation, patient coverage, and possible increased attrition rates. A separate approach to consider would be to videotape the initial learning session provided and make it available to all staff by web so that independent online review and competency exams in NovaLung could be completed.

Introduction of the NovaLung as a treatment option in ICU would require education on:

- Introductions of the technology and how it can assist patient physiology
- Inclusion/exclusion criteria
- Initiation of treatment: Policy & procedures
- Hands on awareness of the device
- Basic care and maintenance of a patient with the NovaLung
- Underlying labs/flow rates/physiological parameters to be monitored
- Troubleshooting management
- Emergency situation management
- Discontinuation/weaning of the treatment: Indicators & procedures

Though management of the NovaLung patient does not require a perfusionist, members of the ECLS support team should be present for insertion, set up, priming and initial operation of the NovaLung until patient stability is reached. They should also be available for weaning and decannulation of NovaLung. Once the patient is stable, the ECLS support team will be available 24/7 for telephone consultation. Staffing considerations should include resourcing a nurse patient ratio of 1:1 if possible. Communication with supporting departments which will be impacted by the use of the NovaLung will need to occur, and include blood services and lab services. Availability of PRBCs, albumin, and Platelets will be important, as will rapid and frequent ABG and blood work checks.