The Autopsy Pathologist and the Extra Corporeal Membrane Oxygenation (ECMO) Related Autopsy

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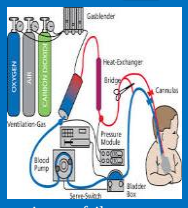
It Started with a Little Hope

- **Year:** 1974; **Place:** Orange County Medical Center, (OCMC) CA
- **Prologue:** A pregnant woman from Baja, Mexico, with aspirations to offer her offspring a better life, crossed the border & headed for L.A.
- She went into precipitate labor and delivered a baby.
- **Event:** Baby developed severe meconium aspiration pneumonia with very dismal prognostic chances.
- Robert Bartlett, a thoracic surgeon at OCMC, wheeled an ECMO machine from his lab and hooked the baby to the machine.
- **Outcome:** The baby survived and was named Esperanza or "Hope" in Spanish by the hospital nurses.

Wolfson PJ : The Development and Use of Extracorporeal Membranes in Neonates; Ann Thorac Sug 2003; 76:S 2224-9.

As always a successful event has many claimants, but failures have none



- Claimants to being progenitors of ECMO:
  - 1944 – Artificial kidney developers
  - 1953 – Gibbon – first open heart surgery
  - 1965 – Raskind bubble oxygenator – to support a neonate dying of respiratory failure
  - 1969 – Dorson – cardiopulmonary bypass
  - 1970 – Baffles – support adult with post traumatic respiratory failure
  - In 1971, Donald Hill, a San Francisco Thoracic Surgeon, had used an ECMO on a patient with ARDS

Anecdotal Success to Evidence Based ECMO Use

- Report of NIH sponsored multi-institutional prospective randomized controlled study published in JAMA 1979
  - 90 patients – mostly respiratory conditions randomly assigned to conventional medical therapy or ECMO - Prematurely stopped because 90% mortality in both groups
- Robert Bartlett – 1984 and 1986 – Hosp. Practice & Ann. of Surgery
  - 100 cases of infant on ECMO – 90% predicted mortality, 75% recovered
  - Are baby lungs different, better at self repair, or early Rx start
- University of Michigan's 1992 " Randomized play the winner" technique –
  - 11 treated with ECMO all survived; 1 treated conventional died
- 1989 – Boston Children's study – Adaptive design
  - 19 of 20 (97%) on ECMO survival vs 6 of 10 (60%) on conventional Rx
  - Criticized by readers, NIH to World Medical Association, Helsinki

Ave, Cesar, morituri te salutant!*
(Hail, Cesar, those who are about to die salute you!)

- UK Collaborative ECMO Trial Group. UK collaborative randomized trial of neonatal extracorporeal membrane oxygenation; Lancet; 1996; 348; 75-82.
- UK Collaborative ECMO Trial Group. The UK ECMO trial follow –up to 1 year of age. Pediatrics; 1998; 101; E1.
- Efficacy and Economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): A multi-centric randomized controlled trial. Peek GJ, Mugford M , TiruvoipatiR et al: Lancet; 2009; 374; 1351-63.
- *Wallace DJ, Millbradnt EB & Boujoukos A: Critical Care; 2010; 14; 308.

Extracorporeal Membrane Oxygenation for 2009 Influenza A (H1N1) Acute Respiratory Distress Syndrome; JAMA; 2009; 302 (17); 1888-1895.

- Use of Bi-caval dual lumen catheter for adult veno-venous extracorporeal membrane oxygenation. Javidhar J, Brodie D, Wang D, Ann Thorac Surg; 2011; 91; 1763-9.

ECMO Indications for Cardiac Support

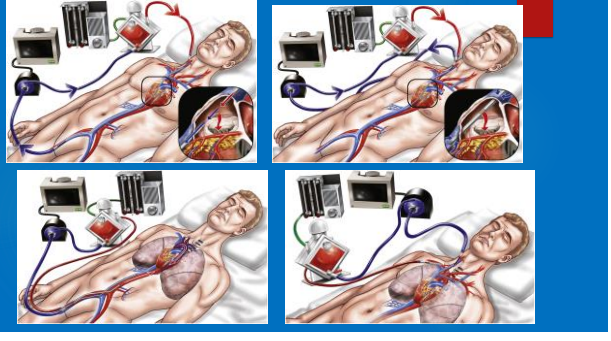
- Cardiogenic shock/ Sev. cardiac failure
  - Acute coronary syndrome
  - Cardiac arrhythmic storm refractory to other measures
  - Sepsis with prolonged cardiac depression
  - Drug overdose / toxicity with profound cardiac depression
  - Myocarditis
  - Pulmonary embolism
  - Isolated cardiac trauma
  - Acute anaphylaxis
- Other related conditions:
  - Post cardiotomy – inability to wean from cardiopulmonary bypass
  - Post heart transplant: primary graft failure or after heart lung transplant
  - Chronic cardiomyopathy
    - Bridge to longer term ventricular assist device support
    - Bridge to decision
  - Periprocedural support for high risk percutaneous cardiac intervention
  - Bridge to transplant

Makdisi G, Wang I-w: Extra corporeal Membrane Oxygenation (ECMO) a review of a life saving technology; J Thorac Dis; 2015; 7 (7); E 166 – E176.

ECMO Indications for Respiratory Support

- Acute respiratory distress syn.
  - Severe bacterial or viral pneumonia
  - Aspiration syndromes
  - Alveolar proteinosis
- Extra corporeal assistance to provide rest to lungs
  - Airway obstruction
  - Pulmonary contusion
  - Smoke inhalation
  - **Vaping Related Lung Injury***
- Lung transplant
  - Maintenance of patients after lung resection or failure of lung transplant
  - Bridge to lung transplant
  - Intraoperative ECMO
- Lung hyperinflation
- Pulmonary hemorrhage or massive hemoptysis
- Congenital diaphragmatic hernia
- Meconium aspiration

Makdisi G, Wang I-w: Extra Corporeal Membrane Oxygenation (ECMO) a review of a life saving technology; J Thorac Dis; 2015; 7 (7); E 166 – E176.



Differences between VA and VV ECMO

VA ECMO	VV ECMO
Provides cardiac support to assist systemic circulation	Does not provide cardiac support to assist systemic circulation
Requires arterial and venous cannulation	Requires venous cannulation
Bypasses pulmonary circulation	Maintains pulmonary blood flow
Decreases pulmonary artery pressures	
Could be used in Rt. V. failure	
Lower perfusion rates needed	Higher perfusion rates are needed
Higher PaO2 is achieved	Lower PaO2 is achieved
ECMO circuit in parallel to H & L	ECMO circuit in series to H & L

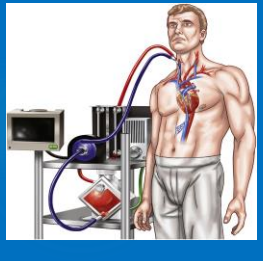
Makdisi G, Wang I-w: Extra Corporeal Membrane Oxygenation (ECMO) a review of a life saving technology.

COMING SOON TO AN AUTOPSY ★★ROOM NEAR YOU★★

Nouveau Indications for ECMO use

- **Aeromedical evacuation of cases with acute lung injury**
  - Allan PF, Osborn EC, Bloom BB et al: The introduction of ECMO to Aeromedical evacuation; Military Med; 2011; Vol 176; p 932 – 937.
- **Awake ECMO as bridge to lung transplantation**
  - Fuehner T, Kuehn C, Hadem J et al: Extracorporeal Membrane oxygenation in awake patients as bridge to lung transplantation; Am J Respir Crit. Care Med; 2012; 185; 7; 763-768.
- **To facilitate organ recovery**
  - Shapiry IM & Muiesan P: Regional perfusion by extracorporeal membrane oxygenation of abdominal organs from donors after circulatory death: a systematic review; Liver trans; 2013; 19; 1292 - 1303.
- **Support in trauma cases**
  - Mokire JM, Kelsey M , Rut Y et al: ECMO for critically ill adults in emergency department: history current applications and future directions; Crit Care; 2015; 19; 431 – 439.

Nouveau Indications for ECMO Use



The ECMO market expected to reach US $346 m by 2024; US domination of current ECMO market 40% in 2015

- Improvements in biocompatible materials used in the devices
- "Tip to Tip" heparin coated circuit
- Heat exchanger built in to circuit or hypothermia inducer if brain trauma is suspected
- Smaller, more compatible and portable machines
- Use of software programs and feedback loops to monitor, predict and correct: anticoagulation, acid base balance and circuit issues like recirculation; pump pressures and training about safe operation and trouble shooting of all equipment

ECMO Use – Past, Present And Future

ECMO 1 (1990 -2008)	ECMO 2 (2009 – 2017)	ECMO 3 (2018 – 20??)
Sedation, paralysis	Awake Spontaneous breathing	Awake, Ambulatory
Intubated	Tracheostomy, extubate	Extubated
Resting ventilation settings	CPAP	Off Ventilator
Specialist care 24 hours -7 days a week	ICU Nurse, ECMO Support Group	Conventional care, weeks or home care for months
Lung recruitment	Watch and wait	Spontaneous breathing
Bleeding complication major	Bleeding complication minor	No anticoagulation

Bartlett R.H.: ECMO: The next ten years; Egyptian Jnl Crit Care Med; 2016; 4; 7-10

A limited glossary of ECMO acronyms

- **ALIRT**- Acute Lung Injury Rescue Team
- In the same cohort: Lung protective ventilation
- E**CCO2R** – **(ECCO2R)** Extracorporeal carbon dioxide removal
- **ECLA** – Extracorporeal Lung assist system
- **ECLS** –Extracorporeal Life Support Systems
- **ECPR or E-CPR** – Extracorporeal cardiopulmonary resuscitation
- **ELSO Registry** – Extracorporeal Life Support Organization
- **Hybrid ECMO circuit** - Double lumen cannula for VA & VA ECMO
- **VV and VA ECMO** – Veno-Venous and Veno-Arterial ECMO
- **LVAD & VAD** – Left ventricular assist device & Ventricular assist device

Continuing Training for ECMO Staff

- Training, education & certification of a broad based inter professional team including practice drills of the entire team of:
  - Registered Respiratory Therapists (RRTs) and Registered Nurses (RNs)
  - Cardiovascular perfusionists
  - Critical Care Unit (CCU) Staff physicians, Residents and Fellows
  - Cardiovascular Surgery (CVS) Staff physicians, Residents and Fellows
- ECLS/ Advances Technologies Education subcommittee
  - Continuing education by subject matter experts on a variety of topics
- Critical care interprofessional ECMO – Performance Improvement Process – Monthly meetings/ discussions

Kotani Y, Honjo O, Davey L, et al: Evolution …, estab.. of program……; Artificial Organs; 2013; 37 (1); 21 – 28.

ECMO RELATED AUTOPSIES ON HOSPITAL CASES AT CCMEO

Age / Sex Autopsy	Indication for ECMO	Type - Duration	Clinical question to be answered at autopsy	Significant ECMO related finding
75 - W Limited	Pulmonary fibrosis	VV 17 days	Appropriate location of catheter Severity of lung disease Remaining infection	Coagulopathy, not excessive
38 - M Limited	Reccurent pulmonary thomboemboli, unknown etiology	VA + V 20 days	Cause and origin of P E Pulmonary vascular disease? Pulmonary infarcts?	Partial occlusion of 2/3 SVC ports with thrombi
50 - W Complete	Pulmonary failure after gastric bypass surgery	VV 2 days	Any intracranial hemorrhage? Source of abdominal hemorrhage Lung condition Was there endocarditis?	Focal thrombosis within femoral catheter tip extending into hepatic vein with liver necrosis Multifocal cerebral white matter Abdominal hemorrhages
47 - M Limited	Acute respiratory failure with hypoxia and hypercapnia	VV 13 days	Why he decompensated rapidly while waiting for lung transplant	None
40 - W Complete	Aspirated food during intubation Developed hypoxia & hypercapnia Developed intracranial hemorrhage	VV 1 day	What cause? Unclear whether about IC He or need for intubation	Rt. Atrial mural thrombus, probably unrelated to ECMO

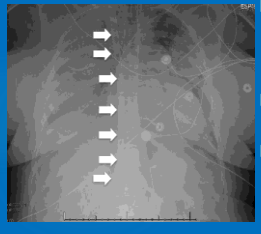
Our recommendations for developing a protocol for requesting autopsies on ECMO cases:

- Renal failure and renal injury occur in about 55% of cases. Work up of medical renal conditions involves extensive immunohistochemistry, something that is not frequently done in the usual variety Medical Examiner case work.
- Hemorrhagic complications occur in 40% of cases and evaluation of coagulopathy is in the domain of specialized Clinical Pathologist. Heparin induced thrombocytopenia leaves no organic lesion that can be identified.
- Infection is a complication in about 30% of cases and hospital bed side is the ideal place for obtaining cultures to identify organism.
- Gastrointestinal bleed is also known to occur due to stress, ischemia and secondary to the bleeding disorders. Again, an organic lesion may not be identified at autopsy.

Our approach for autopsies on ECMO cases:

- A complete autopsy should be advocated. Considering 5 to 10% of causes of death in ECMO cases could be intracranial hemorrhage, a torso only autopsy is inappropriate. Reassurance of the next of kin that all funeral options are possible after the autopsy as is routine in forensic autopsy cases.
- The ECMO cannula and lines should be left in place at the hospital. The cannula should be evaluated in situ at the start of the autopsy to identify appropriate placement and patency and rule out injuries to right ventricle.
- Signs of hemorrhage, thrombosis, ischemia and/or stroke should be sought at the immediate end organs but also peripherally including extremities and brain.
- The migration of the catheter tip to hepatic vein and secondary hepatic necrosis or infarct is a known complication and in situ dissection is the only way to document the condition.
- Malpositioning of the cannula in relation to tricuspid valve should be noted.

NOT EVERYTHING IS CLEAR CUT DESPITE THE ADVANCES IN THE TECHNOLOGY



- Radiological opinions are at best the interpretations of black, white and gray scale images and have their own limitations.
- Reinforces the need for pathological / autopsy evaluation
- Co-training of pathologist with the ECMO team will help communication, formulating the proper questions and modulate the expectations from the autopsy results.

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