Good morning ladies and gentlemen, welcome again to our first ECMO training course. To start off the second session of our ECMO use in ARDS and respiratory failure, I’m going to talk about the use of ECMO in ARDS including those patients who have H1N1 as well as trauma.

When we talk about ARDS it is defined as the PaO2/FIO2 ratio less than 200. It is associated with severe and diffuse injury of the alveolar or capillary membrane of the lungs. In literature it’s been stated to have a precedent of anywhere from 1.5 to 75 cases per thousand person population with the mortality being stated anywhere from 30 to 70 percent. When we look at the causes of ARDS we have a primary cause which is a direct insult to the lungs including that of pneumonia, aspiration inhalation, drowning as well as a secondary insult where lungs become affected by systemic process including shock secondary to sepsis trauma.

When we look at the effects of the lung with ARDS causes, these lungs have a capillary leak in which these lungs become wet, soggy, heavy and we classify this as these lungs have a noncardiogenic pulmonary edema. With this you can get surfactant depletion and these lungs you get decreased compliance with secondary to collapse and consolidation causing a VQ mismatch.

The general indications of respiratory failure and the use of ECMO when we talk about lung disease we’re asked is the lung disease acute? Has the patient has been on prolonged mechanical ventilation for several weeks? Is the lung disease life threatening as well as is it reversible which is more important? Can we make the patient better by putting this patient on mechanical support on VV
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ECMO? And most importantly have we tried other conventional therapies such as nitric oxide oscillator or prone position and most importantly one should note that ECMO does not treat the underlying pathology?

So we tried to maximize these patients before considering putting on ECMO the way we maximize oxygenation as Dr. Arthur Bermudez pointed out earlier in his talk is that we transfuse the patient up to a hematocrit 35%. If the patient hemometrically tolerate we try to diurese these patients, try to dry the lungs out making these patients at dry weight if possible. We also would try sedation as well as a trial of paralytics in order to try to decrease oxygen consumption and utilization therefore hopefully increasing saturations as well as attempt other salvage therapies including nitric oxide, prone positioning and oscillator.

Next we when we talk ECMO in respiratory failure how do we cannulate our patients? We cannulate our patients on VV ECMO support, this is purely respiratory support, this support has no human manic support at all, basically we take blood from the venous system and we put it back into the venous system. These patients are cannulate periphery and by being able to cannulate this patient peripherally we can do it right in the ICU generally under local anesthetics, but most of these patients are critically ill and already are sedated and may be paralyzed at that time. Also we can use less strict anticoagulation on these patients because the patient’s heart is still ejection so you are less concerned about clot formation.
When we talk about cannulating our patient on VV ECMO peripherally we have dual stage cannulation and Dr. Bauma will tomorrow talk about this in a lot more detail and that we cannulate the patients in the right IJ using arterial cannula which is – we try and cannulate intervenous cannula in the right femoral vein. There are times when the right IJ vein may be thrombose or unusable and then we might cannulate these patients on femoral-femoral VV bypass using the right artery or insert the right femoral vein and the left femoral vein.

Over the last few years the Avalon cannula has come out and we’ve started to use this cannula in this patient population and to date in our ARDS patient population we have used this on 12 out of our 50 ARDS patients. And which this is a single lumen but dual lumen cannula which has both the arterial and venous port, and basically we are drawing blood from the IVC and from the SVC and we are putting blood back into the – arterialized blood back into the arterial port which is put in at the level of the right atrium to the tricuspid valve.

The other type of respiratory support that we could use in respiratory failure is a pump for support called the Nova Lung. Of note this is a pump so there is no pump associated with this. This pump works by using the patient’s own profusion pressure, the blood pressure. So if these patients are hypotensive this is probably not a good pump to use, as well these patients have significant hypoxic respiratory failure you will only get modest increase of oxygenation where you get clearly good CO2 removal. These patients are cannulated from the – in the femoral area from the femoral vein to the femoral artery.
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So next we decide who gets ECMO in using our criteria. We try to look at patients who have been cannulated less than 10 days, but we do make exceptions. We don’t always abide by that, if somebody is otherwise young and healthy and single organ failure, they are cannulated for 14 to 17 days, after consultation with our other colleagues we may decide to go ahead and put that patient on ECMO. We also look at those patients who have a significant shunt greater than 30%, and with this they have decreased compliance as well as life-threatening hypoxemia and hypercapnia. We also before putting these patients on ECMO usually point out we try recruitment efforts in that we try to increase the P, increase in _____ or saturations. Also we try to increase the mean airway pressure as well by using other ventilator modalities.

So who doesn’t get ECMO? So if you have an unrecoverable respiratory issue and you are not a candidate for lung transplant, so if you are a 70 year old lady who comes in with pulmonary fibrosis who is not a candidate for transplant secondary to end stage renal disease on hemodialysis, this patient we cannot make better so should not be a candidate for mechanical support on VV ECMO. Those patients who have CPR with evidence of tissue malperfusion as well as suspicion of anoxic brain injury should not be candidates for cannulation. If the patient has an incurable disease such as a malignancy or liver cirrhosis, those patients should not be candidates for cannulation as well as those patients who present or has a recent CNS bleed. We look at some of the relevant contraindications, we look at severe obesity in that severe obesity makes it very difficult to cannulate patients. So we should look at the patient, if the patient is severely obese whether or not we could
actually physically get them cannulated, and if we do get them cannulated whether or not we are going to even achieve adequate flows with these patients.

Those patients with chronic organ dysfunction such as renal insufficiency or renal failure as well as those patients who may have some contraindications to anticoagulation such as a patient who may have recently been admitted with a large GI bleed, we have to consider whether or not those patients will or will not be a candidate for ECMO support secondary to the potentiality of using anticoagulation on our patients for the ECMO support. Advanced age, so our cutoff has been 65 years of age, we do make exceptions after consultation with our colleagues whether or not we are going to cannulate these patients who are over 65 years of age as well as those patients who have prolonged mechanical ventilation which our cutoff is 10 days but we will go longer in that.

So how do we optimize these patients after being supported on VV ECMO? And simplistically we feed these patients, we feed them early, we try to get the nutritional stores up to par or keep them up par if they are already there. I think it’s very important in the patient progressing getting better and coming off ECMO as far as their long term rehabilitation. We sedate these patients but we do not snow these patients in that we use modest amount of sedation that allows us to be able to manage the patients clinically in the ICU. We try to avoid the complications of long term high levels of sedation that can occur with the critically ill ICU patients if possible.
As far as antibiotic management, we don’t use antibiotics prophylactically. We use antibiotics according to our clinical suspicion and that of our microbiological evidence of the patient. What we don’t want is we don’t want patients treated prophylactically in that they develop a super infection down the road during their ICU course.

And we do invasive procedures such as bronch the patients. We bronch the patients probably their most procedure are that we do in the ICU, it’s because these patients are sedated generally, are not able to cough and clear secretions, or secretions causing mucous plugging therefore can increase VQ mismatch, decrease in oxygenation and by cleaning the patient’s lungs out to clean out the mucous we can hopefully allow and provide better oxygenation to some of these patients. And we also trach these patients, if we see these patients are not going to come off ECMO early or they are going to have a prolonged mechanical ventilation. And about 50% of our ARDS patients end up being trached in the patients that we looked at.

And we wean the patients as soon as possible. And how do we wean the patients? We think to ourselves whether or not this patient can adequately support themselves. You know can they come off ECMO? Are they on reasonable event settings such as an NFO2 of 50%, a P of 10, reasonable compliance on the ventilator. Is their chest x-ray improving? If we see all of these things occurring then we turn off our ECMO gases which makes weaning ECMO, VV ECMO very simplistic. We leave the flows off for generally 24 hours, although we’ve made exceptions such as our patient who was cannulated for almost 8 weeks, we held off on decannulating her for 72 hours.
And what we see is that once we turn the gases off we see if we do indeed have a PA, CCO PA catheter in we see if the SVO2 has dropped to reasonable levels where the oxygenation, the saturation has remained acceptable. But if the saturations fall to unacceptable levels then we know that the patient’s shunt is still too excessive and we elect to go back on gases. Again, continuing with the approach of these ECMO patients once we have them decannulated we continue to wean these patients, wean sedation, wean ventilator support, continue nutritional support and try to get these patients optimized again to rehab as soon as possible.

So when we look at the ELSO Registry, which is a retrospective review, reviewing over the last 20 years since 1990 to 2010. I want you to note that this is a voluntary registry, so it may not incorporate what actually is going on in the world of ECMO but it does give us an idea of the trend. And here you can see the Annual Respiratory Adult Runs over the last 20 years and you see this, this peak here in 2009 which one could surmise that this is probably the emergency of H1N1. And in this Registry once they broke them down by the diagnosis, again you can see that viral pneumonia had a reasonably long run but it had the best survival in this registry database.

I’m not going to belabor this point. When we look – we go back and we look at whether or not ECMO has been a proven benefit in ARDS respiratory failure as Dr. Arthur Bermudez so eloquently went through the review of the literature earlier this morning. But again in the 1970s, late 1970s you have the NIH trial which basically showed a terrible mortality of 90% in both groups. In the 1980s
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you had at ECO,R done by Gattinoni over in Italy which also did not show any benefit in survival as well as a lot of these studies were stopped secondary to massive bleeding. In the 1990s you had Morris’s trial that looked at the push control inverse ratio of ventilation in the ECO,R and there was also no survival benefit. And then you had Peek’s trial coming out in 1997 in which he looked at patients on ECMO and he did see a survival in these patients of about 66%.

And then we kind of come to the gold standard that everybody mentioned which was the CESAR trial and looking at ARDS support for respiratory failure ARDS. And it’s been pointed out that patients, 180 patients, 90 patients went to the ECMO arm, only 60 of these patients did get ECMO where 90 patients went to the conventional ventilation arm. It was a multi-centered randomized trial, the Murray score was 3 with a pH that was less than 7.2. And what this study showed is that in the ECMO arm that they had a 63% survival.

And here is actually the Australian data that was published in JAMA in 2009 of the first outbreak of H1N1. This data was actually published before all the outcomes could be determined of these patients but what they did see in their published data is that patients, of the 68 patients that were – who went to the ECMO arm, they had a 71% survival in this group.

There is a paucity of trauma data in looking at support of ECMO in trauma patients, but this is a study that came out in 2010 from Germany, and they looked over a 3 year period of adult patients with severe trauma associated with cardiopulmonary failure. As you can see, the entry scores of
these patients were extremely high as well as the PAAO2, the FIO2 ratio was very low in these patients, so these patients had severe ARDS. These patients also had significant issues as one would expect in significant multitrauma, a lot of issues with bleeding. And what they showed in this retrospective review is that 60% of these patients survived ECMO support, and of these 10 patients 30% were cannulated on veno arterial ECMO where 70% was cannulated on VV ECMO. And one thing about this study as well because of the issues with bleeding they did not use Heparin in their study on these patients and they did not see any evidence of thromboembolic events or issues with clotting formation in the circuit.

Now we’ll talk about our 10 year experience looking at ARDS, which is going to include H1N1 population over the last 2 years as well as – or 2 ½ years as well as our trauma patient population. When we looked at our ARDS patient population this particular slide does include H1N1 patients. We had a total number of patients of 50. Their mean age was 43. They were split about 50/50 between men and female, underlying diseases that these patients came in with included cardiovascular, which was the highest at 18, 36% as well as diabetes at 22%. Some of these patients were immunocompromised, which means that these patients were on Cephalotomize, Prograf or CellCept or any other high potent immunosuppressant not related to transplant. And we also had 4 patients who did have a lung transplant previously but the respiratory failure was not associated with primary graft failure. The causes of ARDS, most of our patients developed ARDS secondary to pneumonia which included H1N1 patient population.
And as you can see here, when we looked at our pre and post ECMO ABGs that these patients had a significant PAO2, the FIO2 ratio, the mean ECMO days was 10 and of these patients about 90% were cannulated on VV ECMO. And 68% of these patients were weaned successfully from ECMO.

When we look at the ventilator days, a lot of our patients, about half of these patients, were actually cannulated within the first day of becoming acutely ill in mechanical ventilation. When we look at some of the complications, some of the hard complications were bleeding which included mostly GI bleeding, some neurological issues which included seizure, stroke as well as encephalopathy, as well as cardiac complications which mostly included just atrial fibrillation. We also had about 16% of our patients who developed hepatic dysfunction and about 38% of the patients developing renal failure in this patient population.

The interesting thing about the survival curve is you can see here at about 30 days you know what we saw was our mortality at about – survival at about 64%, and as we go through the next year we have very little drop-off which tells me that we can pretty much surmise that if the patients can make it past 30 days that their one year survival is going to be fairly – fairly good.

When we broke down our H1N1 ARDS data out from our standard ARDS data we had a total of 16 patients. A little bit younger patient population with a mean age of 39. About two-thirds of the patients were male as compared to female. It’s a little bit healthier patient population than our combined ARDS patient population. Patients were longer on ECMO, length of stay was – hospital
stay was pretty much the same and these patients were successfully weaned off ECMO about 69%.

Again, as you can see from some of the characteristics from looking at their pre and post ECMO gases they also had severe or significant ARDS. And most of these patients were actually cannulated in the first 24 hours of mechanical ventilation. Again, the complication rate was pretty much the same as their overall ARDS ECMO population.

Again, looking at the survival curve of these patients, again looking at the 30 day mortality here we can pretty much – the survival here we can pretty much state that again there is very little drop-off after 30 days in this patient population and if they can survive past 30 days we can pretty much get them through the course. And most of these patients if they survive past 30 days and make it out of the hospital end up having as you saw in some of the pictures that were shown by Dr. Bermudez going back to normal everyday living.

When we looked at our trauma patient population, probably one of the largest that I could find, we had a total of 23 patients over the last 10 years. As one would expect it’s a little bit younger patient population than our other ARDS patients, and they were about split 50/50 between men and female and some of the underlying disease processes, the most leading one was cardiovascular including cardiomyopathy, coronary artery disease status post CABG as well as hypertension, hyperlipidemia. Most of these patients were cannulated on ECMO secondary to pulmonary contusion or acute respiratory failure unrelated to pulmonary contusion. They had a fairly high, significantly high APACHE score of 24.4 and most of these patients trauma was secondary to MVA.
Well we saw in this patient population that the ECMO time which was in hours and means was about 96.5. We saw that the length of stay at the hospital was the longest, which one would expect in patients with multiple poly-trauma of 67 days and that about 50% of these patients were successfully weaned off of ECMO. In this split between Veno-Venal ECMO and Veno-Arterial ECMO was about 65% Veno-Venal and 35% Veno-Arterial. Again, the complications of these patients included renal failure and of the patients who developed renal failure 48% of the patients ended up going on hemodialysis. Infection was also a big risk in these patients as well.

Again looking at the trauma survival curve again, what we see is that here at 30 days the survival of these patients, there’s a pretty steep drop-off in that 30 days, it kind of – you get a linear curve out which again supports that if these patients can make it past 30 days of survival that they have a pretty good chance of long term survivability and outcome.

And now just to go through an anecdotal case that we had, this is a 35 year old gentleman who presented really to an outside facility with really no past medical history. He complained of about a week of lower back pain and leg pain, leg swelling and what brought him into the emergency room at the outside facility was extreme pain with paresthesias as well as now the inability to bear weight and to ambulate. At the outside facility in the ED he was found to be hypotensive, tachycardic and anemic, they started, begun resuscitations there and he was transferred to UPMC Emergency Room.
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for further management where they continued the resuscitation as well as was started on Levophed for refractory hypotension.

Some of his pertinent laboratory data included his potassium was mildly high at 5.2, he was in acute renal failure with a creatinine of 2.2, lactic acidosis of 10.4 and of note his CPK was only 87. On exam his abdomen was mildly tender and diffuse, his extremities were very much hypoperfused, edematous, engorged, and he had no pulses femoral all the way to his distal popliteal anterior tibia as well as DP and PT pulses. And on motor exam his proximal muscle groups were weak, which were about 3/5 bilaterally.

And this was a CT scan that he actually was transferred from the outside facility with in which you can see here that he has a fairly large spontaneous retroperitoneal hemorrhage. He has a very small abdominal aorta and as you can see around this aorta that it’s inflamed. And what you don’t see is you don’t see that he has an absence of the IBC at the level of his super renal level. This gentleman also had duplex Dopplers and when he got admitted to the CT ICU which did confirm that he had both iliac and femoral vein thrombosis.

On hospital day # 1 he, we ordered, consulted orthopedics who did compartment pressures on this patient which were fairly high, so he went to the OR for emergent release of his compartments with fasciotomies. In the OR at that time upon induction intubation he had – was complicated with aspiration. He came out and was expiated the next day, clinically did fine from a respiratory
standpoint by going back and forth to the OR for I&Ds, ultimately it was found that his legs were not going to salvageable so he had bilateral amputations at that time.

On hospital day #7 he went back to the OR for again another I&D at which point in time upon induction again he had a very large volume witnessed aspiration in the OR. When he came back out of the ICU to me he was hypoxic, on 100% ________. We were able to make some ventilatory changes, increasing his means and getting his sats up from the 80s to the low 90s, but that was very much short-lived. He developed pulmonary edema, sats fell to the low 80s, we began to try to manually recruit this patient with only being able to obtain sats up to the mid 80s. So at this point in time we did a consult with Dr. Bermudez and we made the decision that we should try to cannulate this gentleman on VV ECMO support.

Interestingly because we could not use his femoral veins we had no other alternative but to use the Avalon cannula for cannulation. Cannulation was done under ultrasound as well as we also were fortunate enough to have anesthesia here who also helped us guide the cannula in by echocardiograph as well and what you see here is the wire coming down into the IVC and here is the cannula coming down into the IVC in good position for the underlying cannula. And this is just a chest x-ray which shows diffuse bilateral air space consolidation and the arrow is basically pointing to the Avalon cannula which had been inserted into the internal jugular vein transitioning all the way down into the inferior vena cava.
So on hospital, subsequent hospital stay he did develop acute renal failure, ended up on CRT and eventually hemodialysis. We also ultimately treated this gentleman as well. He was decannulated on day #14, on day #41 he was actually being able to be transferred to rehab. We were able to get this gentleman decannulated, renal failure recovered, no longer requiring hemodialysis when he was transferred to rehab.

And this is – if I can get it to start here – there we go – this is Bill at day # 100 from the day he was admitted taking his first steps on his prostheses. I think this was pretty significant in A, the rate of his recovery, the fact that he was able to even be on prostheses at 100 days post the day of his admission was pretty remarkable. I think this also points out to us as well although you know there has not been any proven studies that showed a significant – statistically significant benefit in mortality in the use of ECMO, that there is an accumulation of data out there that may state that ECMO would be useful in the patients with, supporting patients with severe ARDS, and that ECMO can impact the survival of these patients who otherwise have a higher predicted mortality. And as the Seizures Trial did point out that if we can timely consult and transfer these patients to an ECMO center that they probably will do better. And as some of our data did point out as well, if we can get these patients past 30 days that the long term survivability is pretty reasonable. And this goes into the with the advances of technology in ECMO. Thank you.