

2018 AmSECT pediatric
October 4-6, 2018 Miami, FL

AmSECT experience

Anticoagulation Management During ECLS Past-Present-Future

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HeartProgram

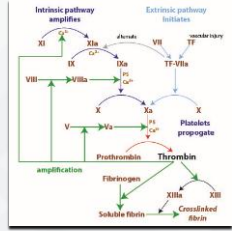
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Anticoagulation Management During ECLS

Heparin

- Discovered 1916
- Current management therapy
 - Imperfect Science
 - Not Standardized
- Past
- Our current practice
- Future



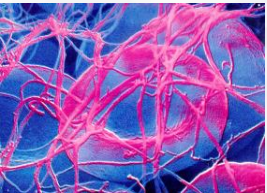
The diagram illustrates the coagulation cascade. The **Intrinsic pathway** starts with Factor XII, which is converted to XIIa. XIIa converts XI to XIa, which then converts IX to IXa. IXa, along with VIIIa and X, converts X to Xa. The **Extrinsic pathway** starts with Tissue Factor (TF) and VII, which is converted to VIIa. VIIa, along with X, converts X to Xa. Xa, along with V and VIII, converts II to IIa (Thrombin). Thrombin converts I to Ia (Fibrinogen) and XIII to XIIIa. Fibrinogen is converted to Fibrin, which is then cross-linked by XIIIa to form Crosslinked Fibrin. Thrombin also converts XIII to XIIIa. The diagram also shows that Factor V is converted to Va, which amplifies the intrinsic pathway.

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Past Heparin Management Techniques

- 1948 WBCT
 - Takes to long
- APTT
 - Not practical or reliable
- 1966 ACT
 - Standard of care 1979
 - 300, 400, 480 Sec. for CPB
- Heparin Dose Response Curve
 - Dosing & reversal



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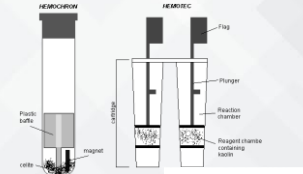
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Activated Clotting Time (ACT)

Advantages

- Quick
- POC
- Low cost
- Simple
 - Whole blood
 - Some dirt
 - Mixed with a stick



The diagram shows two types of ACT testing devices: HEMORON and HEMOTEC. HEMORON is a test tube containing a plastic vial and a magnet. HEMOTEC is a test tube containing a plunger, a reaction chamber, and a reaction chamber containing heparin.

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Activated Clotting Time (ACT)

ACT Disadvantages

- Operator variability
- Testing system
- Factor deficiencies
- Coagulopathies
- Hemodilution
- Platelet dysfunction
- Sample quality

HEMOCHRON: float, magnet

HEMOTEC: plunger, reaction chamber, reagent chamber containing stopper

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Microemboli Production During ECLS

CPB blood filters 1970's

- Decreased cerebral injury
- Microembolic encephalopathy
 - Gaseous
 - Particulate/Solid
 - Thrombi
- ALF Standard of care

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Microemboli Production During ECLS

ECMO Blood filter use

- Unnecessary
 - Closed circuit
 - Less emboli potential
- Dangerous
 - Blood cell damage
 - Frequent filter replacement

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Microemboli Production During ECLS

ECMO Heparin Management

- ACT based
- 180 - 200 sec
- Weeks at a time

Complications (ELSO)

- 26% are neurologic
- Clots most common
 - 52.3% Neonates

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Microemboli Production During ECLS

ECLS safer today

- Advances technology
- Bio-coatings
- Oxygenators / pumps
- ELSO clinical guides
- Heparin management
 - Center-specific
 - Mostly ACT based

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Microemboli Production During ECLS

What is an ACT?

- Depends on who you ask
- No standardization
- Mechanical detection
- I-STAT electrochemical sensor
 - Thrombin substrate conversion

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ACT Validation at NCH

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ACT Comparison Study Two Stations 4 Systems Each

Hemocron Cath-Lab


ACT Plus CPS

Hepon CPB

iSTAT ECMO

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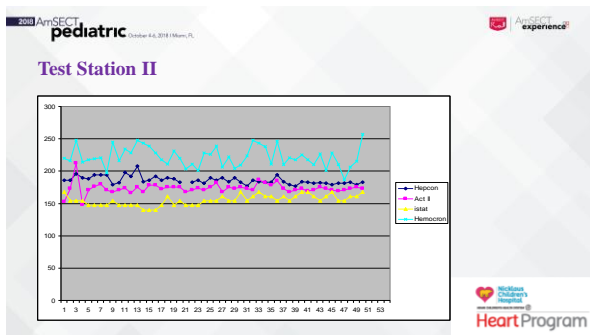
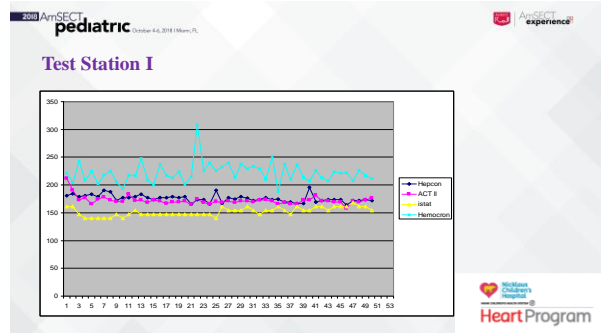
Fresh Heparinized Whole Blood



- 100 simultaneous samples
- 600 ACT tests run
- 800 Data points generated

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ECLS Neurologic Complications

Highest in cardiac Patients.

- Worst in neonates
- Seizures 7.2%
- Infarction 3.5%
- CNS Hemorrhage 11.1%
- Most Underreported**

WJCCM World Journal of Critical Care Medicine

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Neurologic complications and neurodevelopmental outcome with extracorporeal life support

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Exclusive Anti-Xa Titration Anticoagulation Protocol

Anti-Xa based heparin management

- Is feasible
- Decreased blood sampling
- Less Heparin adjustments
- 50% (11/22) Survival

Anti-Xa Directed Protocol for Anticoagulation Management in Children Supported With Extracorporeal Membrane Oxygenation

*E. Gianni Orlowski, James A. Ayres, J. Bruce C. Gossett, F. James C. Lane, M. Dan Pappas**

Background: Heparin is the standard of care for anticoagulation in children with ECMO. However, the current standard of care is based on a limited number of studies, and there is no consensus on the optimal heparin management strategy. The purpose of this study was to evaluate the feasibility and effectiveness of an anti-Xa directed protocol for heparin management in children supported with ECMO. Methods: A retrospective analysis of 22 children who were managed with an anti-Xa directed protocol for heparin management while on ECMO. Results: The protocol was feasible and resulted in a 50% survival rate. There was a significant decrease in the number of blood samples drawn and heparin adjustments compared to the standard of care. Conclusion: An anti-Xa directed protocol for heparin management in children supported with ECMO is a feasible and effective strategy that results in decreased blood sampling and heparin adjustments, and improved survival.

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Exclusive Anti-Xa Titration Anticoagulation Protocol

Bleeding & transfusions associated with

- Thrombotic complications
- Circuit/Oxygenator change-out
- 32% (7/22) Required 1 Oxy/Circuit change
- 11 total occurring at median 93 hours
- 54% (7/13) Postcardiomy Oxy/Circuit change
- 100% Mortality (7/7) Oxy/Circuit change
- 27% Mortality No Oxy/Circuit change

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NCH Current Practice Microemboli Prevention

Strategies

- Maximized hemostasis management
- Prevent stagnant flow fields
- Maintain laminar blood flow
- Reduce foreign surfaces
- Limited circuit port access
- MicroClave IV connector
- All fluids given IV & Filtered
- Integrated ALF



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NCH Coagulation Management

Quantitative

Qualitative

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Viscoelastic Testing Systems

TEG

ROTEM

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Viscoelastic Testing

TEG / ROTEM

- Graphs are similar
- Only POC that evaluates clot strength
- Time to fibrin formation
- Clot stability
- Clot lysis
- Platelet function
- Fibrinogen function

a Normal
R, K, MA, Angle/Normal

b Anticoagulant/hemophilia
Factor deficiency
R; K=Prolonged;
MA; Angle=Decreased

c Platelet Abnormal
Thrombocytopenia
R = Normal; K=Prolonged;
MA=Decreased

d Fibrinolysis (LX, DK, or tPA)
R = Normal;
K = Normal;
MA=Continuous decrease
LY30>7.5%; WBCLD>97.5%;
LY60>15.5%; WBCL60>95%

e Hypocoagulable
R, K=Decreased;
MA; Angle=Increased

f D.I.C
Stage I
Hypocoagulable state with
secondary fibrinolysis

g Stage II
Hypocoagulable state

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Viscoelastic Testing Decision Tree


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Thromboelastography (TEG)

- **Global hemostatic function**
 - Platelet function
 - Fibrinogen function
 - Clotting factors
 - Heparin effect
- **Disadvantage**
 - Training needed
 - Manual pipetting
 - Liquid QC every 8hrs
 - Mechanical shock
 - Two channels
 - Difference normal ranges
 - Infants & adults

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ROTEM (Thromboelastometry)



- **Advantage**
 - Auto-pipetting / touch screen
 - Liquid QC weekly < cost
 - Mechanical shock resistant
 - 4 channels
 - Requires less blood

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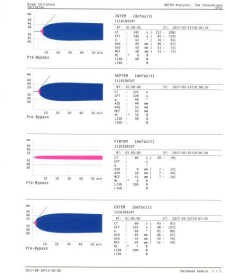
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ROTEM (Thromboelastometry)

INTEM

- Coagulation is activated via the contact phase (as in the aPTT and ACT). The INTEM is therefore sensitive for factor deficiencies of the intrinsic system (e.g. FVIII) and for the presence of heparin in the sample.



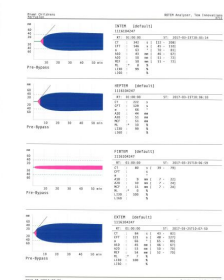
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ROTEM (Thromboelastometry)

HEPTEM

- Coagulation is activated as in INTEM. The addition of heparinase in the reagent degrades heparin present in the sample and therefore allows the ROTEM® analysis in heparinised samples.



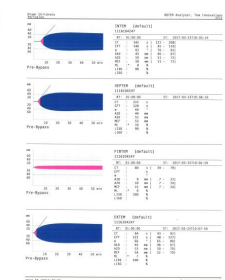
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ROTEM (Thromboelastometry)

FIBTEM

- Coagulation is activated as in EXTEM. By the addition of cytochalasin D, the thrombocytes are blocked. The resulting clot is therefore only depending on fibrin formation and fibrin polymerisation.



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ROTEM (Thromboelastometry)

EXTEM

- Coagulation is activated by a small amount of tissue thromboplastin (tissue factor). This typically leads to the initiation of clot formation within 70 seconds. Thus, clot formation can be assessed within 10 minutes.

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Case revue

ROTEM Pre-CPB

- ACT 186 sec
- INTEM CT prolonged
- HEPTEM CT shorter prolonged
- ATIII level 49
- HMS 3.8 mg/kg
- FFP (1 quad) added to prime

CT	342	s	122
CTP	246	s	46
A	63	mm	70
A10	50	mm	46
A20	50	mm	51
A30	50	mm	51
PL	99	%	
L150	99	%	

CT	222	s	
CTP	128	s	
A	68	mm	
A10	44	mm	
A20	51	mm	
A30	52	mm	
PL	10	%	
L150	99	%	

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Case revue

On CPB only HEPTEM / FIBTEM

- On CPB case end →
- After maximum hemofiltration →
- On CPB after addition of required factors →
- Platelet apheresis (1 Unit) added
- FFP (1 quad) added

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Case revue

During switchover

- Protamine 30mg given
- HMS patient dose
- CPB blood used in support circuit
- Once at full flows
- Fibrinogen (RiaSTAP) 800mg given

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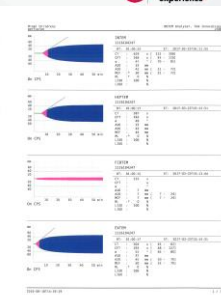
Case review

In CICU 1 hour post-Op

- ACT 200
- CT time prolonged
- FFP (1 quad)
- Platelet apheresis (60cc) added

Heparin is withheld until

- ROTEM results are normal
- ACT is 160
- Bleeding minimal



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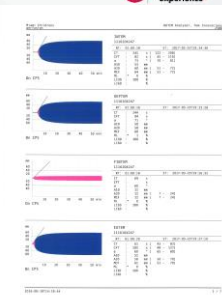
Case review

In CICU 4 hour post-Op

- ACT 162
- CT time prolonged
- No products given

Heparin is withheld until

- ROTEM results are normal
- ACT is 160
- Bleeding minimal



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Case review

In CICU 7 hour post-Op

- ACT 150
- Bleeding minimal
- Heparin started 10 unit/Kg/hr

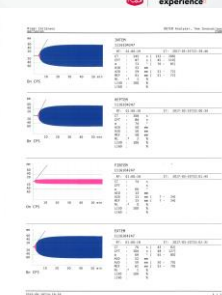



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Case review

In CICU 8 hour post-Op

- INTEM CT prolonged
- HEPTEM CT normal
- ACT 152
- ATIII 52
- AT3 given (Thrombate)
- Heparin 10 unit/Kg/hr








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Case review

In CICU 15 hour post-Op

- INTEM CT time prolonged
- HEPTEM normal
- ACT 163
- ATIII 91
- Heparin 20 unit/Kg/hr






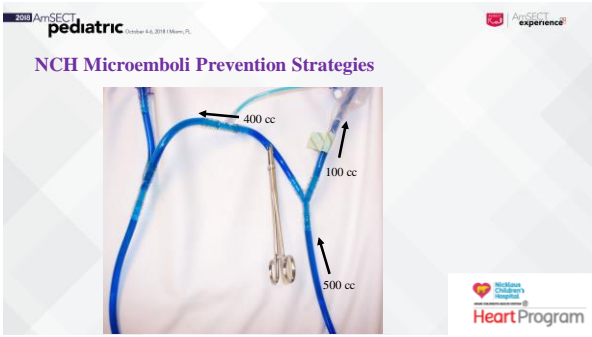
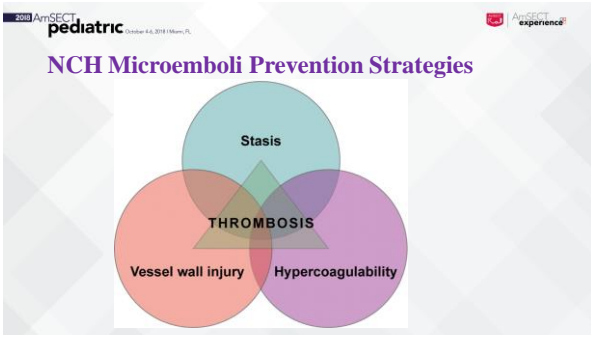






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Case review

In CICU 42 hour post-Op

- INTEM CT time prolonged
- HEPTEM normal
- ACT 161
- ATIII 62
- Heparin 20 unit/Kg/hr
- Off support 44 hours post-op

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Gaseous Micro-Emboli Prevention



■ Intravenous filter



■ MicroClave IV connector

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NCH Microemboli Prevention Strategies



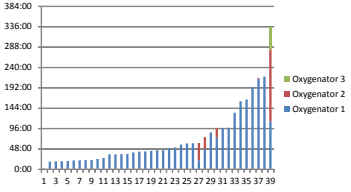
GAPPOV[®] FX Family of Oxygenators
 The GAPPOV[®] FX Family of Oxygenators is designed to provide efficient gas exchange while minimizing microemboli formation. The design features a large surface area and a low flow resistance, ensuring optimal patient outcomes.




GAPPOV[®] FX Family of Oxygenators with Integrated Arterial Filter
 This advanced design integrates an arterial filter to provide an additional layer of protection against microemboli, ensuring the highest level of patient safety.

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Baby FX Oxygenator Longevity

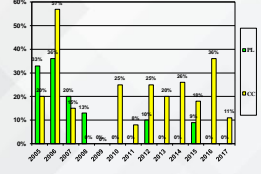


The chart displays the longevity of three oxygenator models (Oxygenator 1, 2, and 3) over a 39-day period. The y-axis represents longevity in hours, ranging from 0.00 to 384.00. Oxygenator 3 (green) shows the highest longevity, reaching approximately 384 hours by day 39. Oxygenator 2 (red) reaches about 192 hours, and Oxygenator 1 (blue) reaches about 144 hours.



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NCH FX / Affinity Longevity & Outcomes (2011-2017)



The bar chart shows the percentage of cases requiring oxygenator/circuit changes (SHD) for various oxygenator models from 2011 to 2017. The y-axis represents the percentage of cases, ranging from 0% to 60%. The x-axis lists the oxygenator models. The SHD percentages are: 2011 (30%), 2012 (35%), 2013 (25%), 2014 (25%), 2015 (25%), 2016 (25%), 2017 (25%).

- 79 CPS using FX Oxy (48% SHD)
- 55 Postcardiotomy (44% SHD)
- 24% (13/55) required oxy/circuit changes
 - 9 increased sweep requirement
 - 3 decreased Blood flow
 - All 3 on in OR using Baby FX
 - 1 Affinity pump (noise)
- 26 Post from CPB in OR (50% SHD)
 - 21% (5/26) required oxy/circuit changes



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Future POC Hemostasis Management Systems

- Fully automated
- Sample vial fits into cartridge
- Avoids sample manipulation
- Automated functional test

TEG 6s



ROTEM Sigma



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Anticoagulation Management During ECLS

Conclusion

- Coagulation Management is complicated and imperfect
- POC Viscoelastic Testing is beneficial
- Postcardiotomy patients at highest risk
- Arterial blood filters during ECLS should be considered

