Use of Blood Lactate Measurements in the Critical Care Setting

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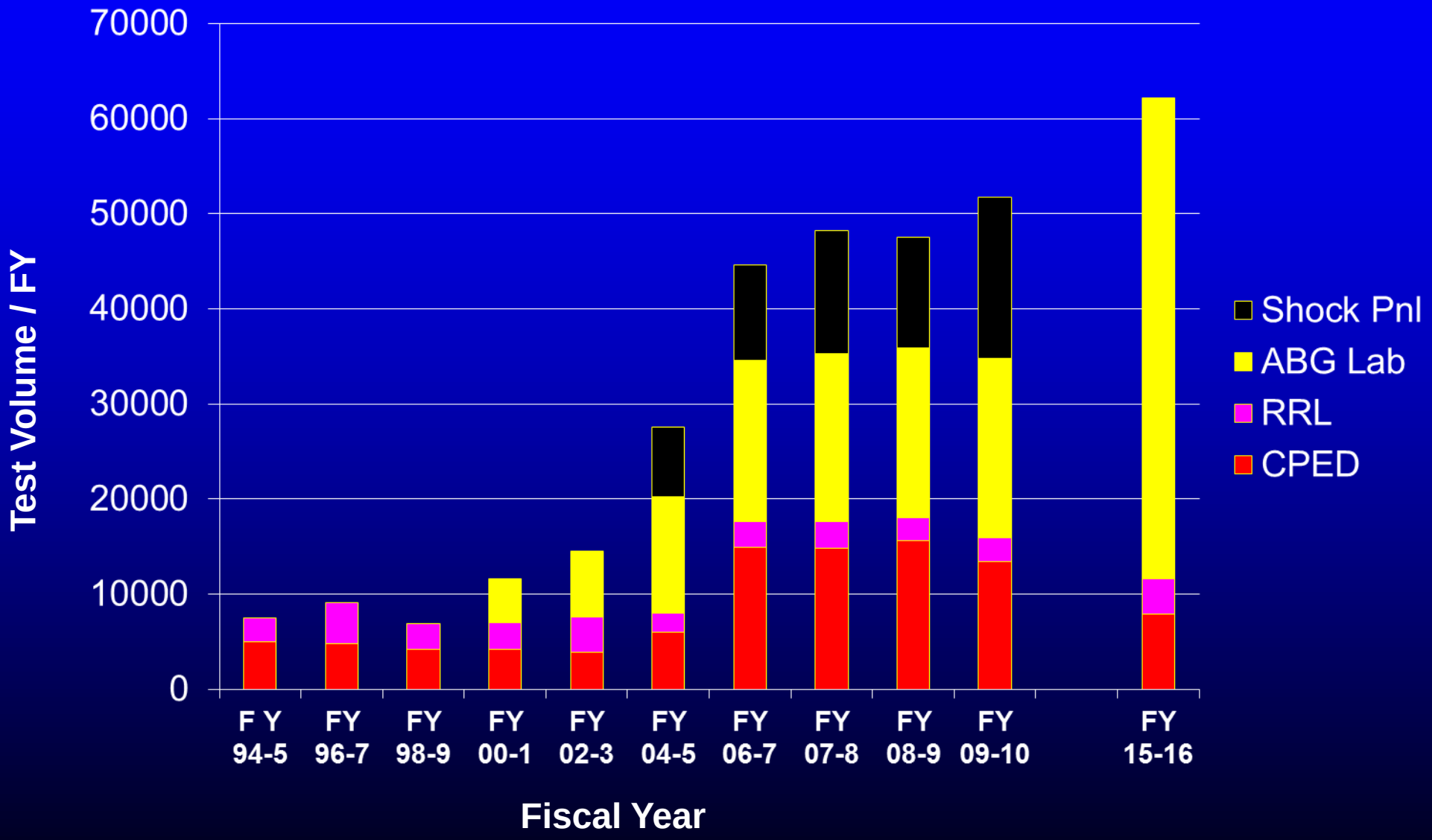
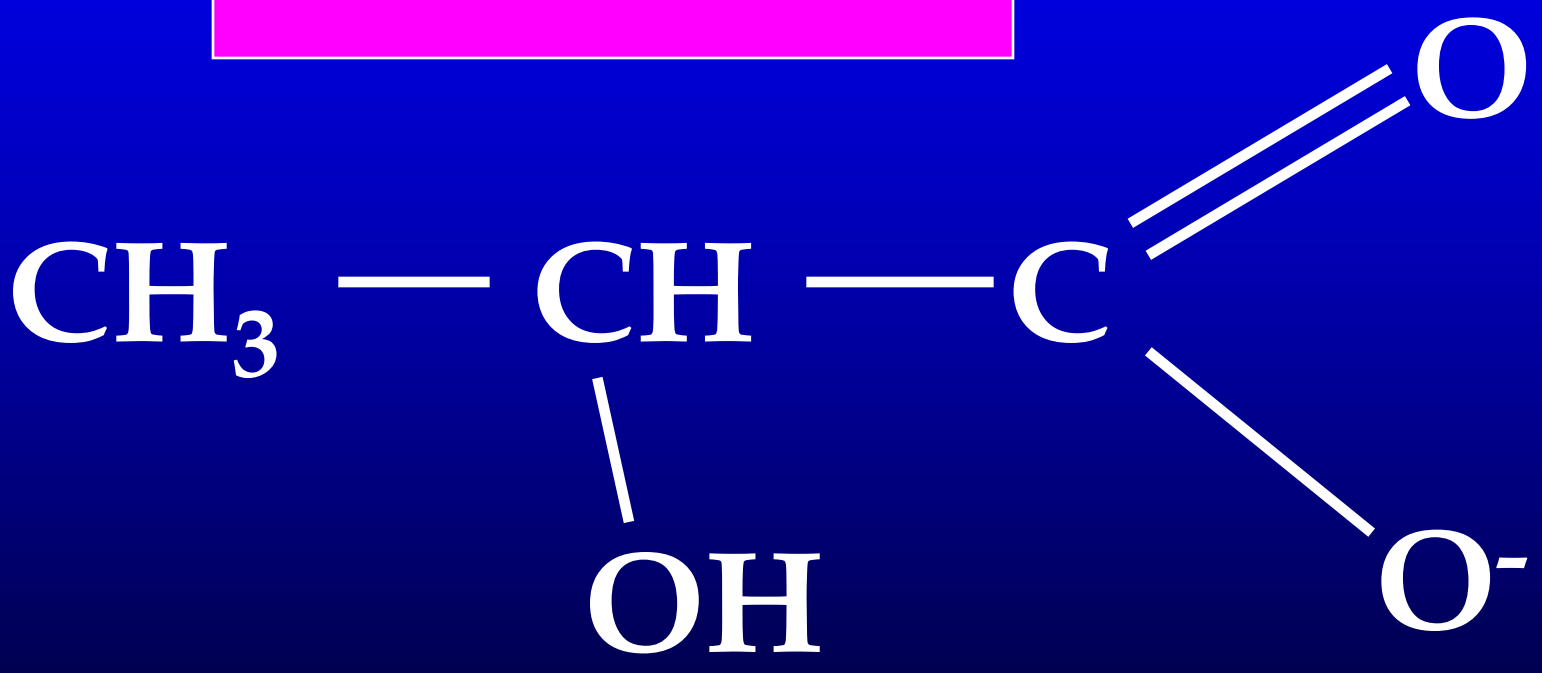
Objectives

- The biochemical mechanisms and clinical processes that can increase blood lactate.
- The clinical implications of an increased blood lactate in surgery, ECMO, in the ED, and in sepsis.
- The general timing sequence of lactate measurements for monitoring patients in critical care.
- The stability of lactate in blood with and without stabilizers.
- When and where POC measurements of blood lactate are useful.

Lactate Testing at Duke Medical Center



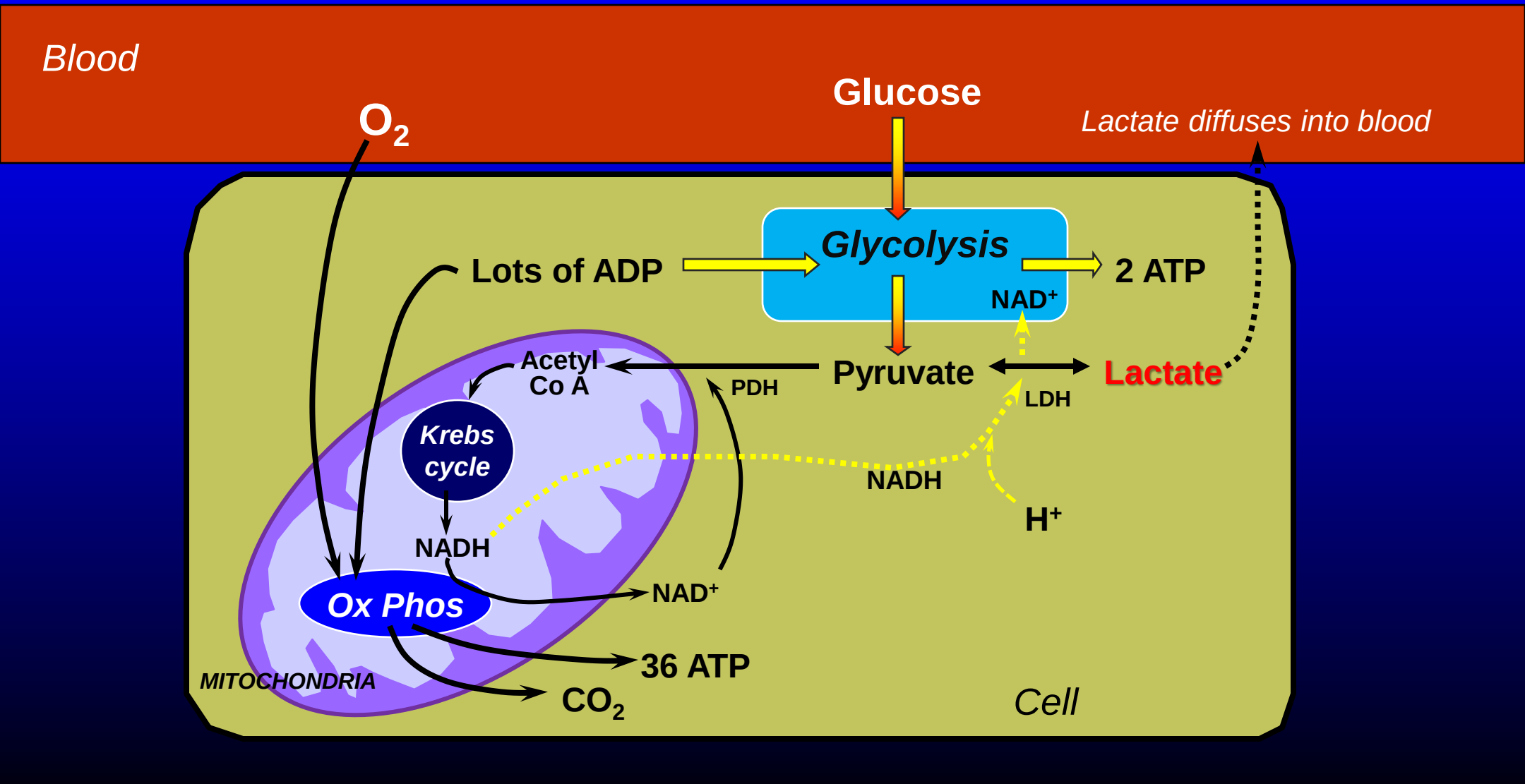
Lactate



Production of Lactate from Pyruvate:

Directly Depends on Ratio of NADH/NAD+

Indirectly Depends on Supply of Oxygen



The Production of Lactate from Pyruvate Actually Consumes Acid

Reaction	Net gain/loss of acid
glucose $\longrightarrow$ 2 pyruvate + $2H^+$	produces 2 H^+
2 pyruvate + $2H^+$ $\longrightarrow$ 2 lactate	consumes 2 H^+
ATP + H_2O $\longrightarrow$ ADP + $HPO_4^=$ + H^+	produces 1 H^+

See: "Biochemistry of Exercise-Induced Metabolic Acidosis". Am J Physiol Integr Comp Physiol 2004; 287: R502-R516

What Processes Can Elevate Blood Lactate?

- Normal RBC and muscle cell metabolism: exercise.
- Inadequate oxygen delivered to tissues. Sepsis
- Increased rate of glycolysis: fever. Sepsis
- Decreased rate of clearance or removal:
  - Liver, kidney damage. Sepsis
- Mitochondrial damage from infections and inflammation: Sepsis
  - O_2 radicals, TNF, cytokines, drugs, etc may be involved.

Clinical Uses for Blood Lactate Measurements: Old and New

- **Monitoring during / after surgery:**
  - **open-heart surgery in neonates**
  - **adult cardiac operations with CP bypass**
- **Monitoring during ECMO.**
- **Triage use in Emergency Medicine:**
  - **trauma patients, chest pain patients**
  - **criteria for ICU admission.**
- **Detecting / monitoring metabolic alterations in sepsis and septic shock.**

Interpretation of Blood Lactate Results

- **≤ 1.8 mmol/L: Normal adult at rest**
- **2.0 - 4.0 mmol/L: Moderately elevated**
- **> 4.0 – 5.0 mmol/L: Seriously elevated?**
- ***But the direction of change may be more important!***

What Does a Blood Lactate Concentration Tell You Clinically?

- In many patients (surgery, trauma, with sepsis, respiratory distress, etc) an elevation may indicate a problem:
  - insufficient oxygen to tissues, inflammation, etc.
- In an emergency setting with multiple patients to treat:
  - Which patient is sicker?
    - Which patients can wait for treatment?
    - Which patients need immediate care?
- Is what you are doing making the patient better or worse?

General Format for Using Blood Lactate Measurements

- **Measure lactate right away:**
  - Lactate normal: GOOD
  - Lactate slightly elevated: Investigate cause; initiate therapy
  - Lactate markedly elevated: Consider more aggressive therapy
- **Measure lactate every 3-6 hours:**
  - Lactate decreasing: GOOD
  - Lactate staying the same: Increase level of therapy
  - Lactate rising: BAD – Consider most aggressive therapy
- **Evaluate after 24 hours:**
  - Lactate normal or close to normal: GOOD
  - Lactate still clearly elevated: Consider more aggressive therapy

Blood Lactate in Pediatric Cardiac Surgery

Blood Lactate Following Pediatric Cardiac Surgery

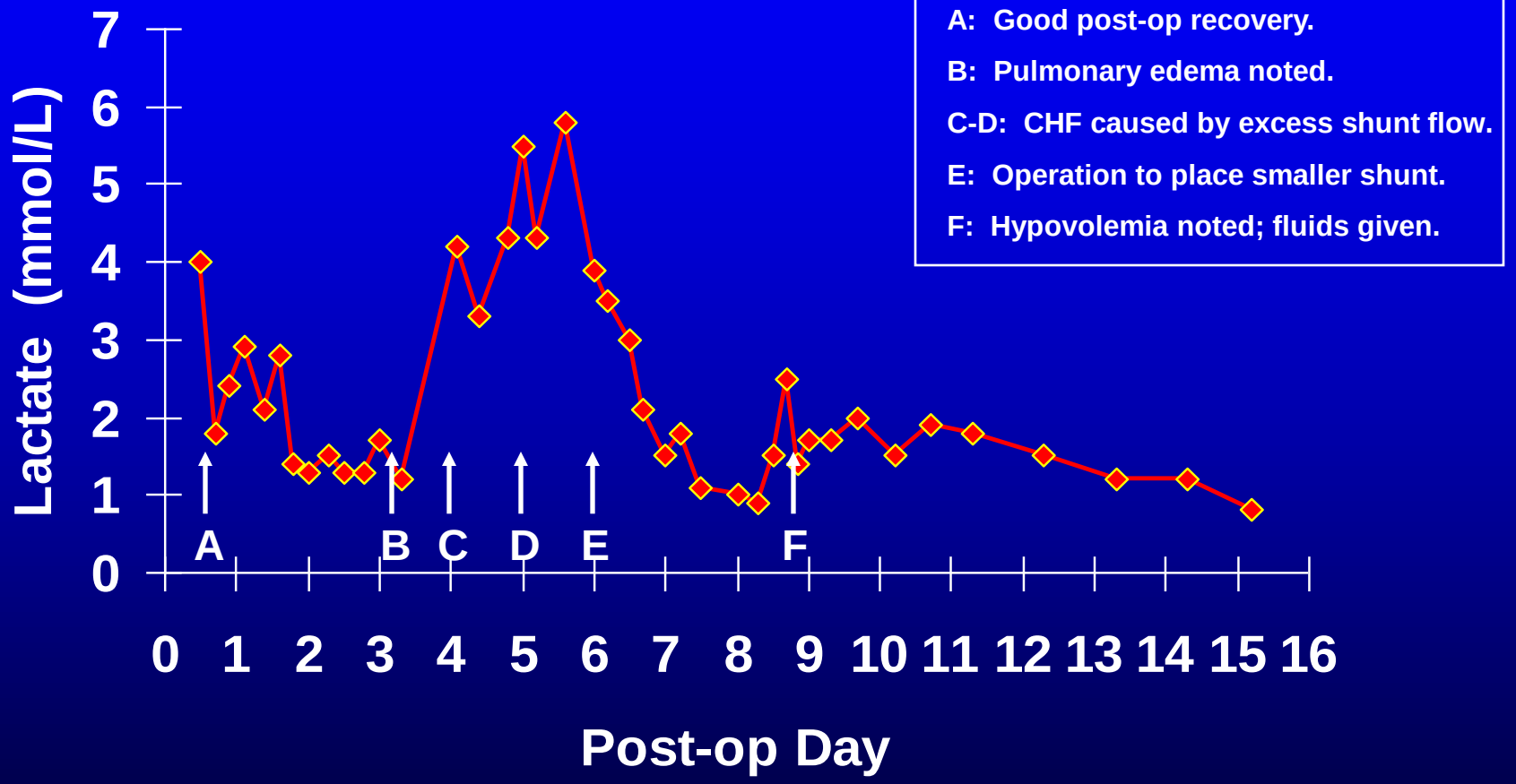
Timing of measurements:

- **Blood lactates are measured after surgery, then every 4-8 hrs after as necessary during recovery.**

Interpretation:

- **Post-surgery lactate of $\geq$ 4 mmol/L generally indicates more intensive care will be needed.**
- **A definite rise in lactate at any time warrants immediate intervention.**
- **After 24 hours, lactate should be normalizing.**

Pediatric Open-Heart Surgery: Closure of Ductus Arteriosus with Placement of Shunt from Aorta to Pulmonary Artery



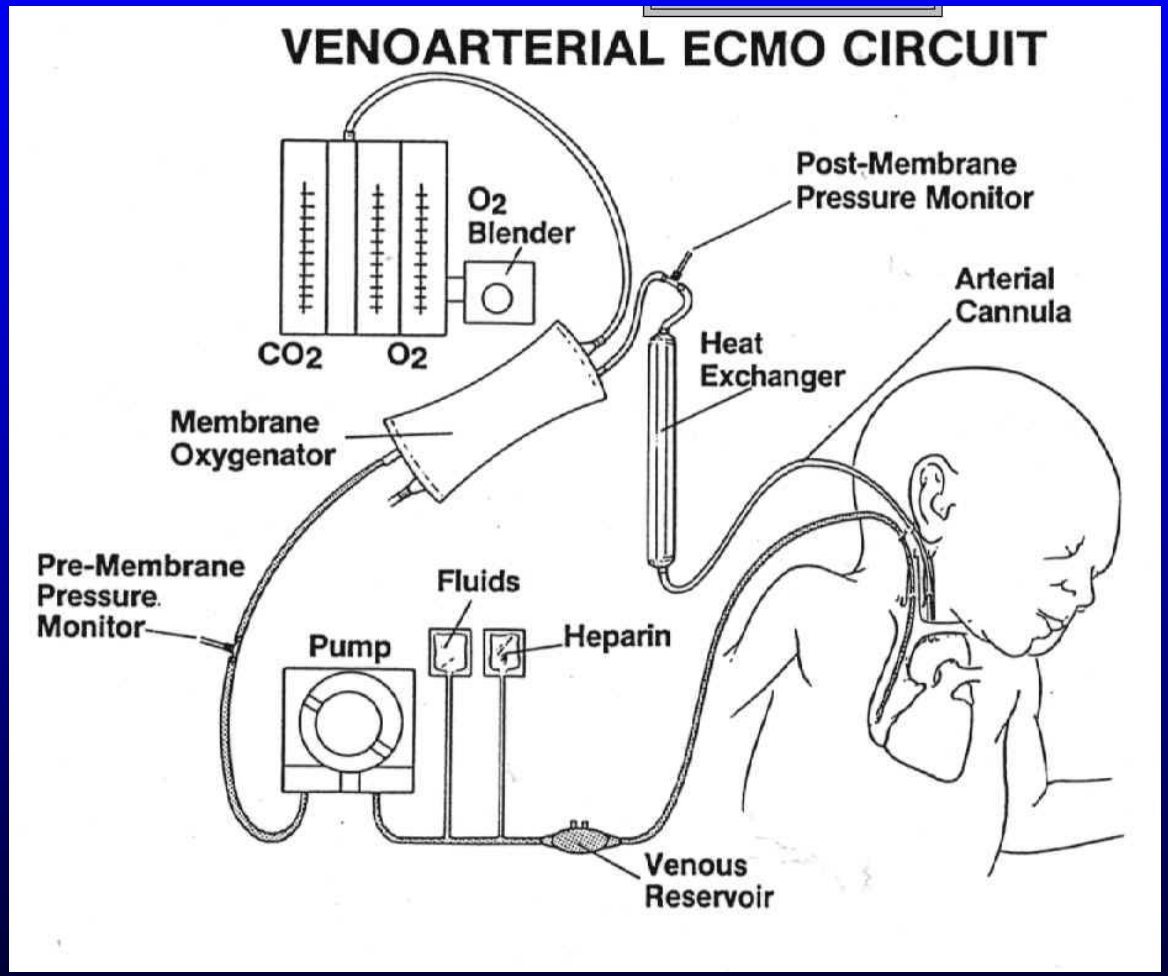
Scand J Clin Lab Invest 1995; 55: 301

Blood Lactate Use in ECMO

(Extracorporeal Membrane Oxygenation)

(ECLS = Extracorporeal Life Support)

ECMO = Extracorporeal Membrane Oxygenation



Interpretation of Blood Lactate Results During ECMO

- In questionable cases, lactate measurement can help determine if patient goes on ECMO or not (≥ 5 mmol/L).
- Lactate declining or remaining low during ECMO is good.
- If lactate increases or remains elevated:
  - may increase pump flow, blood volume, or hematocrit.
  - evaluate for cardiac problems.
  - consider changing to veno-arterial ECMO.

Scand J Clin Lab Invest 1995; 55: 301-7.

Blood Lactate in Adult Cardiopulmonary Bypass Surgery

Information Provided by Blood Lactate Measurements In Adult Cardiopulmonary Bypass (CABG) Surgery

Monitoring blood lactate evaluates the complex metabolic state of the patient recovering from cooling, hemodilution, anesthesia, vasoactive drugs, inflammation, coagulopathies, etc.

Principles of Evaluating an Elevated Lactate After Open-Heart Surgery

- **If reperfusion is good, lactate should decline by 1-2 hours after surgery.**
  - **However, lactate declines slowly in some patients.**
- **If lactate remains elevated 1-2 hr after surgery:**
  - **Make sure cardiac output is good.**
  - **Make sure airways are clear.**
  - **Evaluate liver function**
    - » **liver shutdown can diminish lactate removal.**
  - **Look for gut ischemia or peripheral ischemia.**

Case 1: CABG Operation with No Complications
67 yo male; recent Myocardial Infarction

Time	8:40	9:15	10:00	11:15	11:30	12:00	14:00
FI-O_2	0.40	0.40	0.70	0.70	0.21 (RA)	0.21	1.00
pO_2	108	101	210	280	180	45	120
%O_2 Hb	98.5	96.7	99.2	99.6	99.3	84.0	98.8
Hb	11.5	10.8	8.2	8.0	8.2	8.5	10.2
O_2 content	15.7	14.5	11.3	11.1	11.3	9.9	14.0
Lactate	1.2	0.9	1.5	2.5	3.8	4.6	2.5

Patient on pump

Rise in lactate post-op is a relatively normal occurrence.

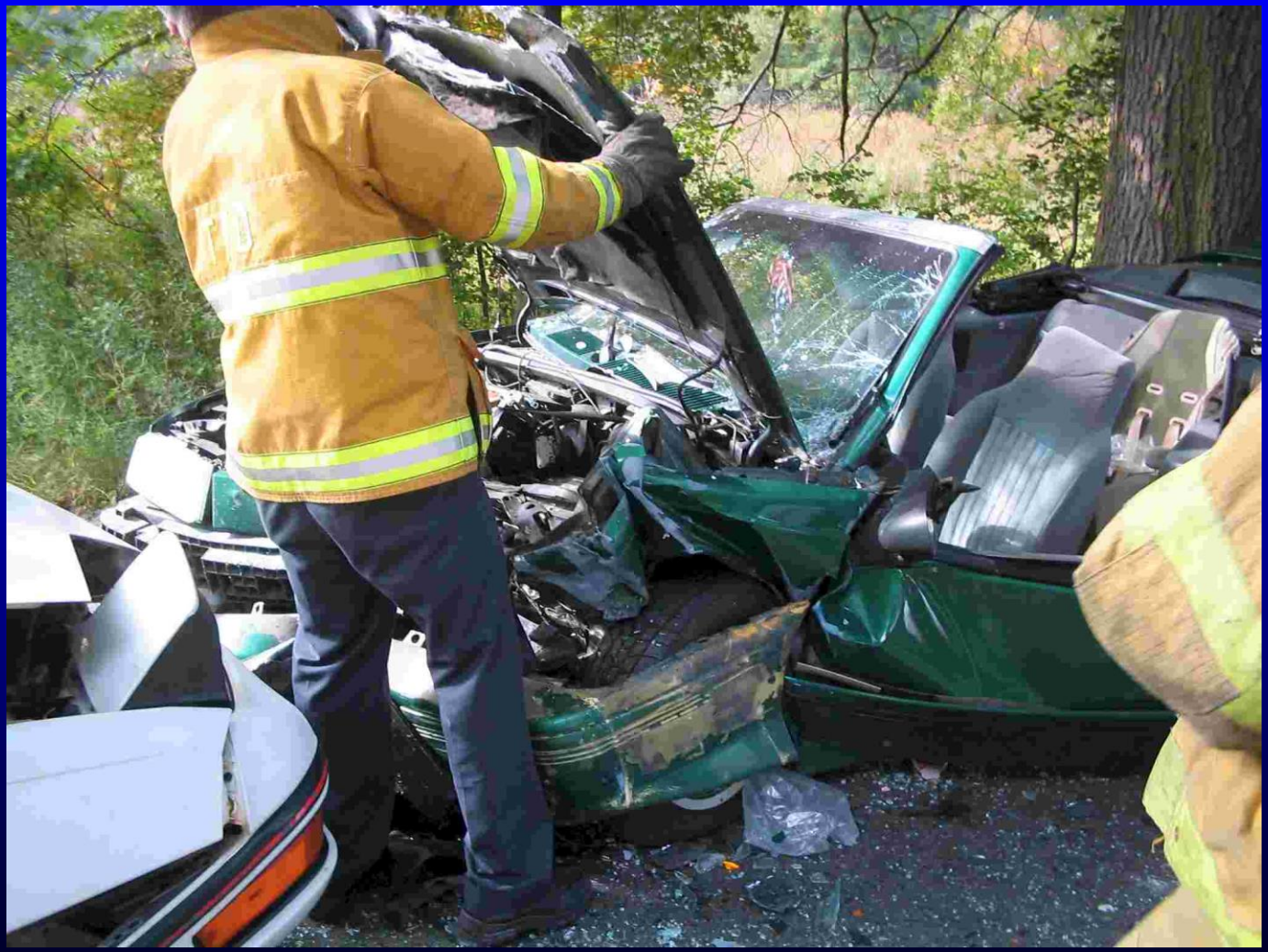
Case 2: CABG Patient With Post-Operative Complications

- 56 year old male underwent open-heart surgery for coronary artery bypass.
- Blood lactates were measured:
  - Lactate during surgery was 3.2 mmol/L.
  - 4 hr post-surgery lactate was 6.1 mmol/L.
- Several parameters were re-checked:
  - Cardiac output was good
  - No evidence of gut ischemia
  - No problems with breathing
  - Poor peripheral pulses were noted in leg.

Case: CABG Patient Post-Op (cont'd)

- **Patient had an intra-aortic balloon pump inserted through femoral artery to increase cardiac output post-op.**
  - **Balloon pump may be constricting blood flow to leg.**
- **Balloon pump was removed from femoral artery.**
- **Lactate measured 2 hours later was 1.7 mmol/L (normalizing).**

Use of Lactate in ED for Trauma and Hypovolemic Shock

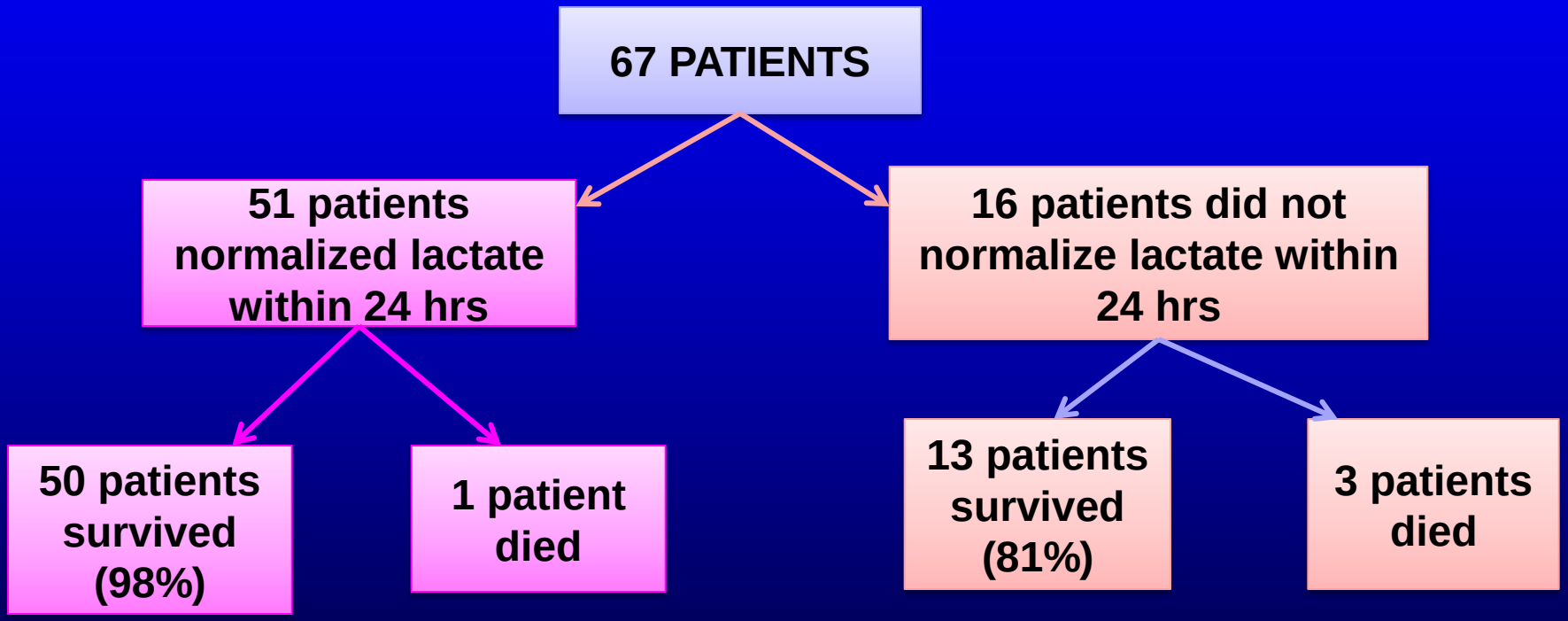


Early Report on Value of Blood Lactate Measurements in Trauma Patients

- **A study of 76 patients admitted to the ICU from either the OR or the ED found that the time needed to normalize blood lactate predicted survival rate of patients:**
  - 100% (27 of 27) survival when lactate normalized in 24 hours.
  - 78% (21 of 27) survived when lactate normalized within 24-48 hours.
  - 14% (3 of 22) survived if lactate did not normalize by 48 hours.

Abramson, et al: J Trauma 1993; 35: 584-589.

Lactate As Predictor of Survival in Trauma Patients



Dr AM Shah; Dept of Anesthesiology; Ganga Hospital; Coimbatore

Blood Lactate Is Also Helpful in ED for Treating Hypovolemic Shock

- **For hypovolemic shock from:**
  - **Bleeding, dehydration, etc.**
  - **Cardiogenic shock**
- **If resuscitation attempts decrease lactate:**
  - **Continue on this course.**
- **If blood lactate stays the same or increases:**
  - **Look for other causes: sepsis, etc.**

Sepsis

Lactate and Sepsis

- Lactate is associated with outcomes in sepsis.
- Initial lactate > 4.0 mmol/L can indicate especially poor prognosis.
- However, hyperlactatemia is observed in patients with and without shock.
  - May be from tissue hypoxia: hypovolemia, shock, vasoconstriction.
  - May be from mitochondrial dysfunction.

New Definitions for Sepsis and Septic Shock

- **Sepsis starts as a systemic infection that leads to unregulated immune and inflammatory responses that can cause life-threatening organ dysfunction.**
  - **Sepsis is common in the ED.**
  - **SOFA score often 3 or above.**
- **Septic Shock defined as:**
  - **Sepsis with especially profound circulatory, cellular, and metabolic abnormalities (SOFA score often ≥ 9).**
  - **Has persistently low arterial BP *after volume replacement* and requires vasopressors to maintain BP ≥65 mmHg.**
  - **Blood lactate >2 mmol/L despite volume resuscitation.**
- **Cryptic Shock:**
  - **Severe sepsis with Lactate > 4.0 mmol/L and systolic BP > 90 mmHg.**

What Are SOFA and qSOFA Criteria?
(quick Sepsis-related Organ Failure Assessment)

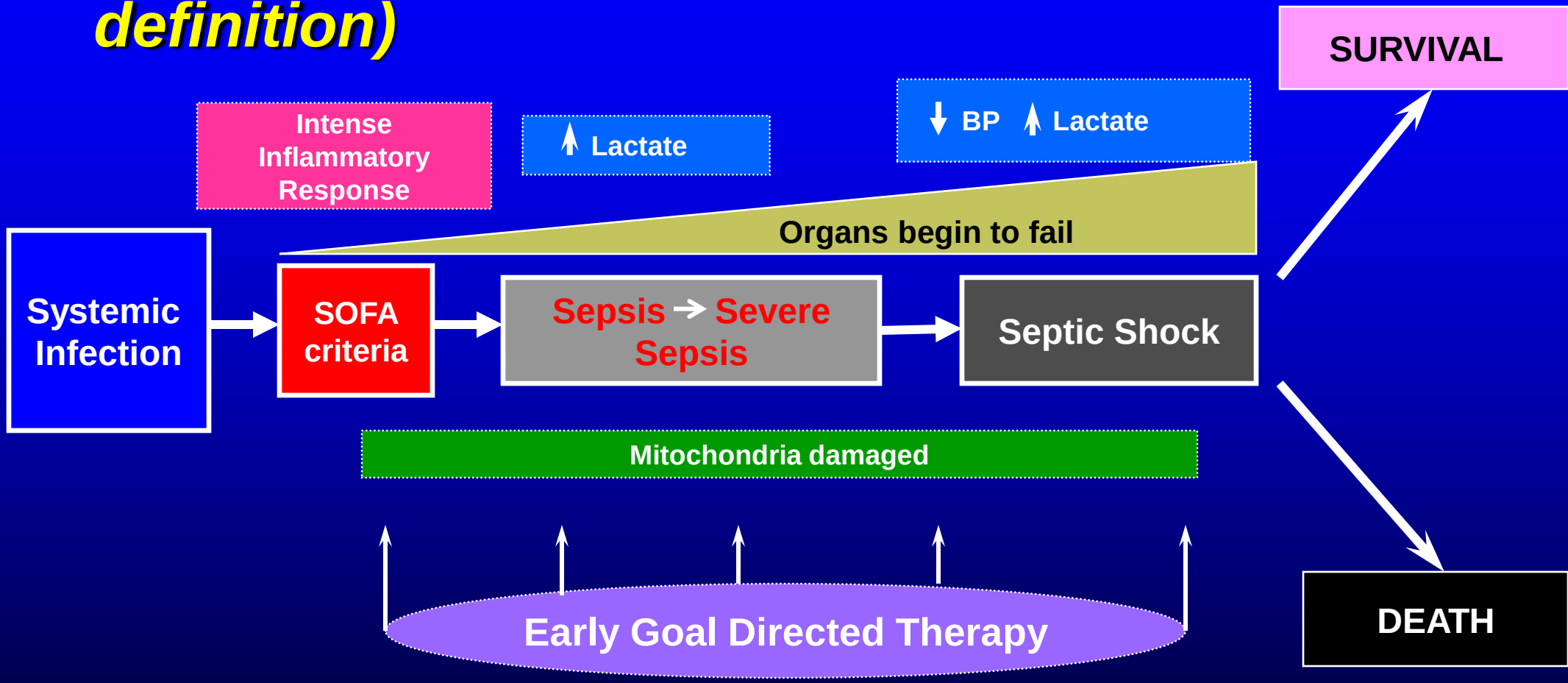
- **SOFA score is related to organ status (4 points each:**
  - **Respiratory (p_aO_2 / FIO_2)**
  - **Mental (Glasgow coma score)**
  - **Liver (Bilirubin)**
  - **Coagulation (platelet count)**
  - **Kidneys (creatinine)**
- **qSOFA score can be used at bedside (1 point each):**
  - **Respiratory rate $\geq$ 22/min (or pCO_2 < 32 mmHg).**
  - **Altered mental acuity**
  - **Systolic BP $\leq$100 mmHg**

Sepsis is a Diverse Syndrome
All these patients could have sepsis:

- **18 yo w/ meningococcemia, coagulopathy, and hypoxemia.**
- **45 yo after visiting SE Asia w/ malaria, new-onset renal dysfunction, and hyperbilirubinemia.**
- **85 yo w/ worsening mental status, diabetes, CHF, anddecreased urine output.**

From JAMA 2016; 315(8): 757-9.

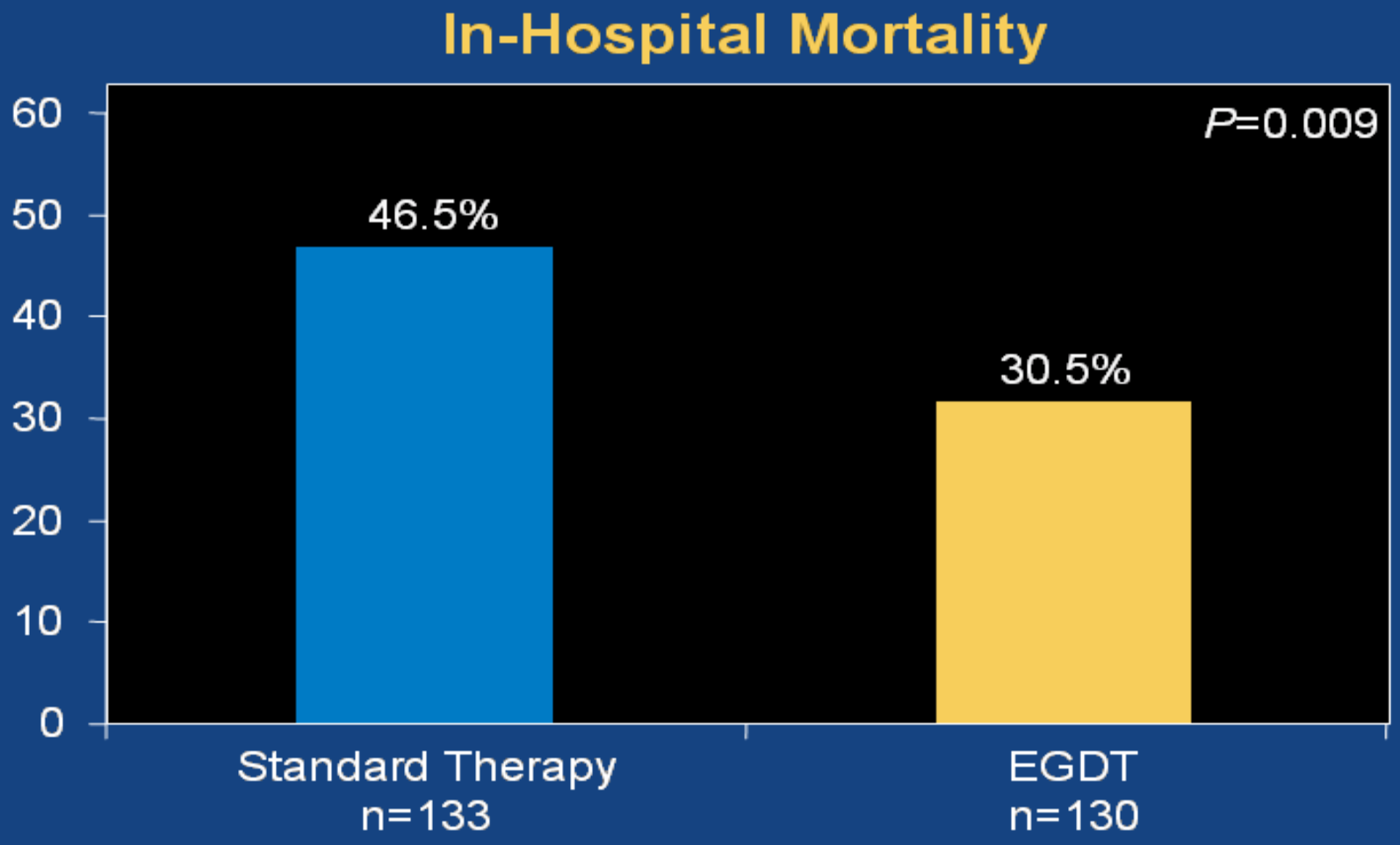
Timeline of Events as Infection Progresses to Sepsis and Septic Shock (new definition)



SIRS = Systemic Inflammatory Response Syndrome

MODS = Multiple Organ Dysfunction Syndrome

EARLY GOAL-DIRECTED THERAPY: RESULTS

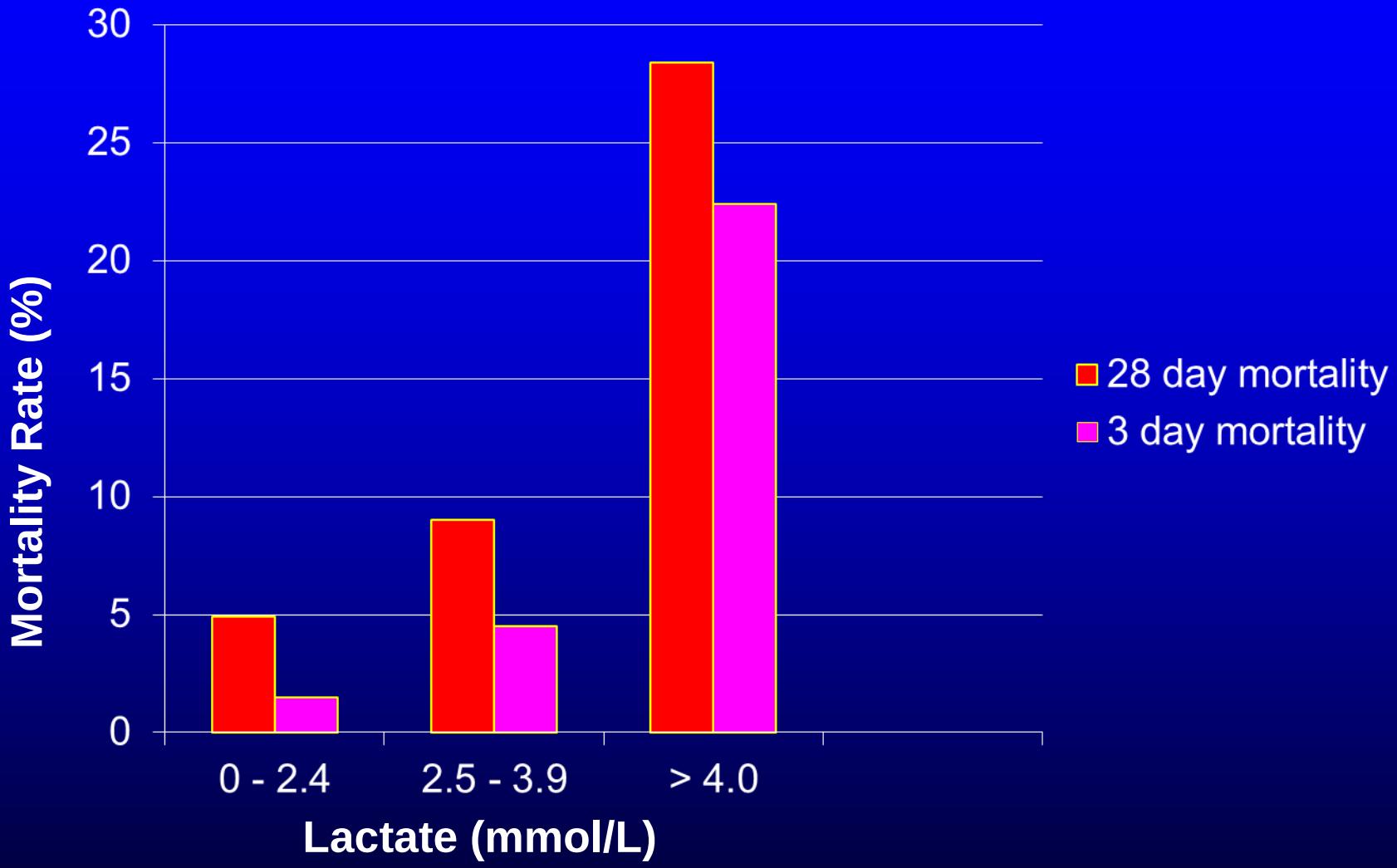


Rivers E, et al. *N Engl J Med.* 2001;345:1368-1377.

3- and 6-Hour Bundles in Goal Directed Therapy Protocol for Sepsis in the ED

- **Do within 3-Hours to identify patients likely to have sepsis:**
  - **Order arterial or mixed venous lactate.**
  - **Order blood cultures: bacteria or virus.**
    - » **Measuring procalcitonin may be helpful.**
  - **Administer broad spectrum antibiotics.**
  - **Give fluid bolus if hypotensive or lactate >4 mmol/L.**
  - **Order CBC, urinalysis, CAT scans, X-rays, etc as appropriate.**
- **Do within 6-Hours:**
  - **Administer vasopressors if BP is low and unresponsive to fluids.**
  - **Remeasure lactate; Adjust antibiotics if culture results available.**
- **Options if hypotension persists and/or lactate remains $\geq$ 4 mmol/L:**
  - **Give red cells to achieve $S_{cv}O_2 \geq 70\%$ or $S_vO_2 \geq 65\%$**
  - **Consider mechanical ventilation.**

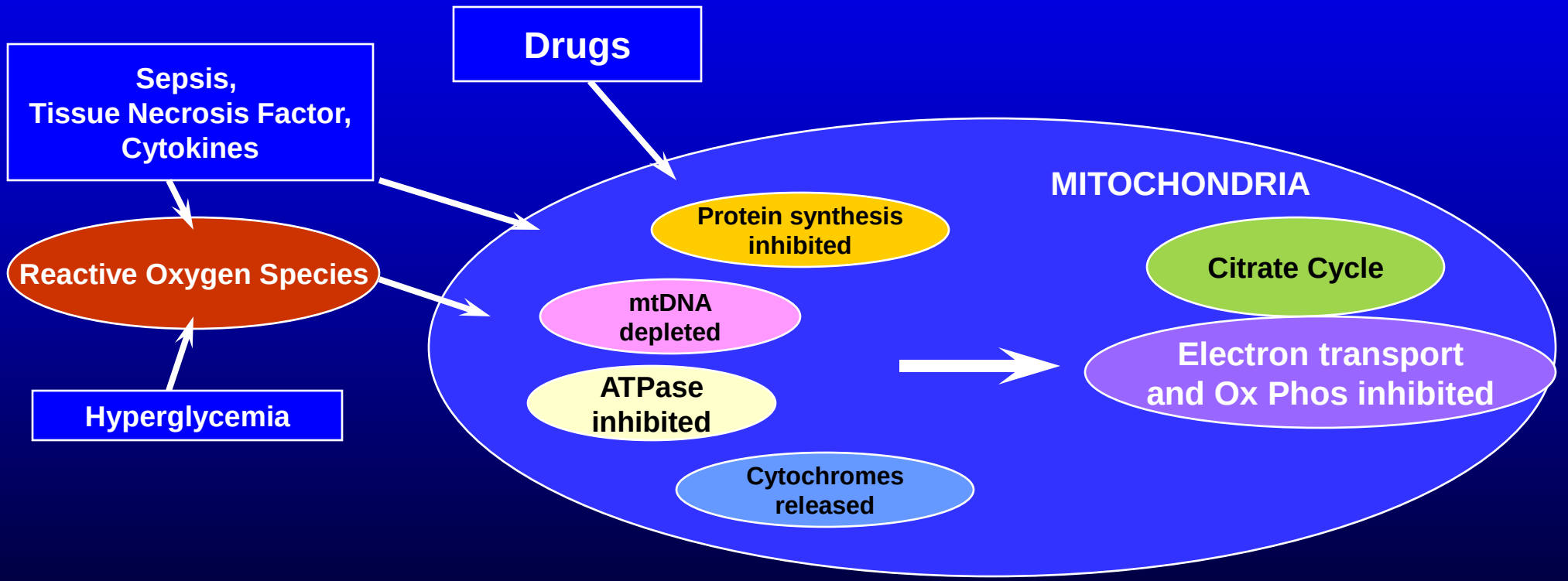
Blood Lactate as Predictor of Mortality in ED Patients with Sepsis



Shapiro NI, et al. Ann Emerg Med 2005; 45: 524-528.

There Are Many Ways to Lose Your Mitochondria

By Drugs, Cytokines, Oxygen Radicals

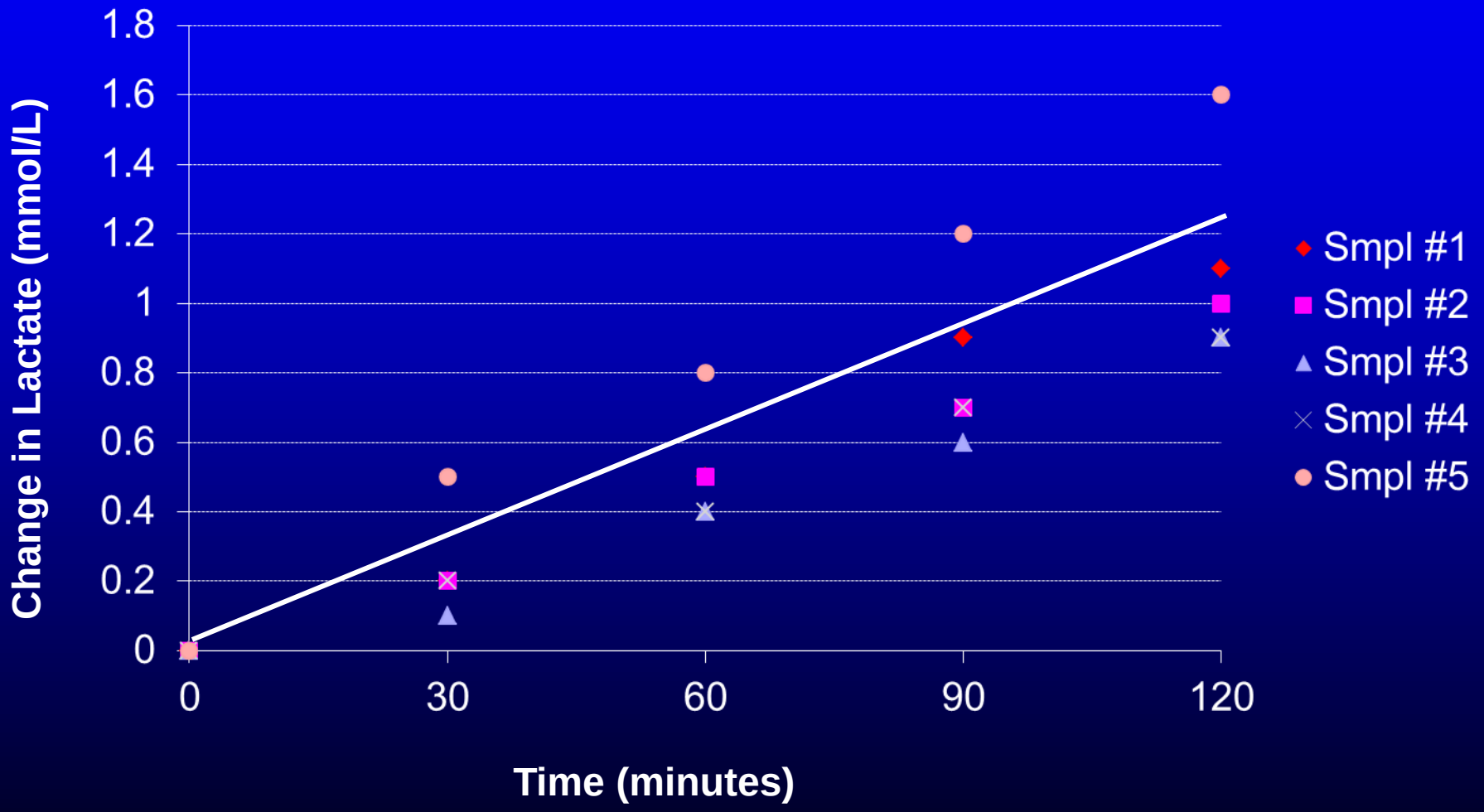


Increase in Lactate (mmol/L) in Blood Containing No Additive or Fluoride / Oxalate

Sample	Temp	Additive	Time	Mean increase in Lactate (mmol/L)
plasma	4-23 °C	F / Ox	8 h	< 0.03
plasma	RT	none	2 h	0.10
WB	RT	F / Ox	2 h	0.10
WB	ice	none	60 min	0.10
WB	RT	none	30 min	0.30 (~1%/min)

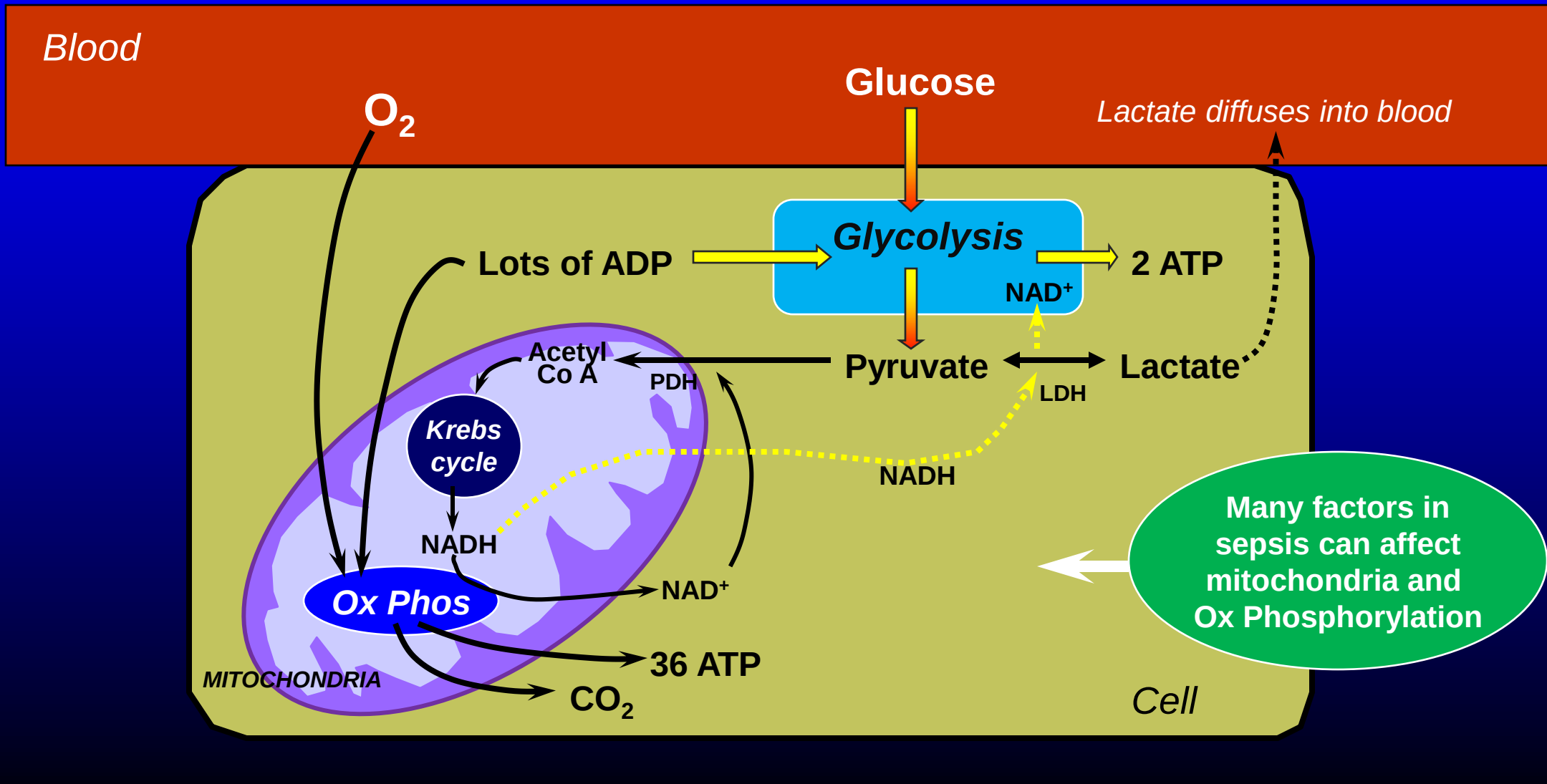
From Westgard, Clin Chem 1972; Toffaletti, Clin Chem 1992; and Astles, Clin Chem 1994

Lactate Changes in Heparinized Blood Gas Samples at Room Temp



Production of Lactate from Pyruvate:

Directly Depends on Ratio of NADH/NAD$^+$
Indirectly Depends on Supply of Oxygen



Summary of Issues with Blood Lactate Measurements

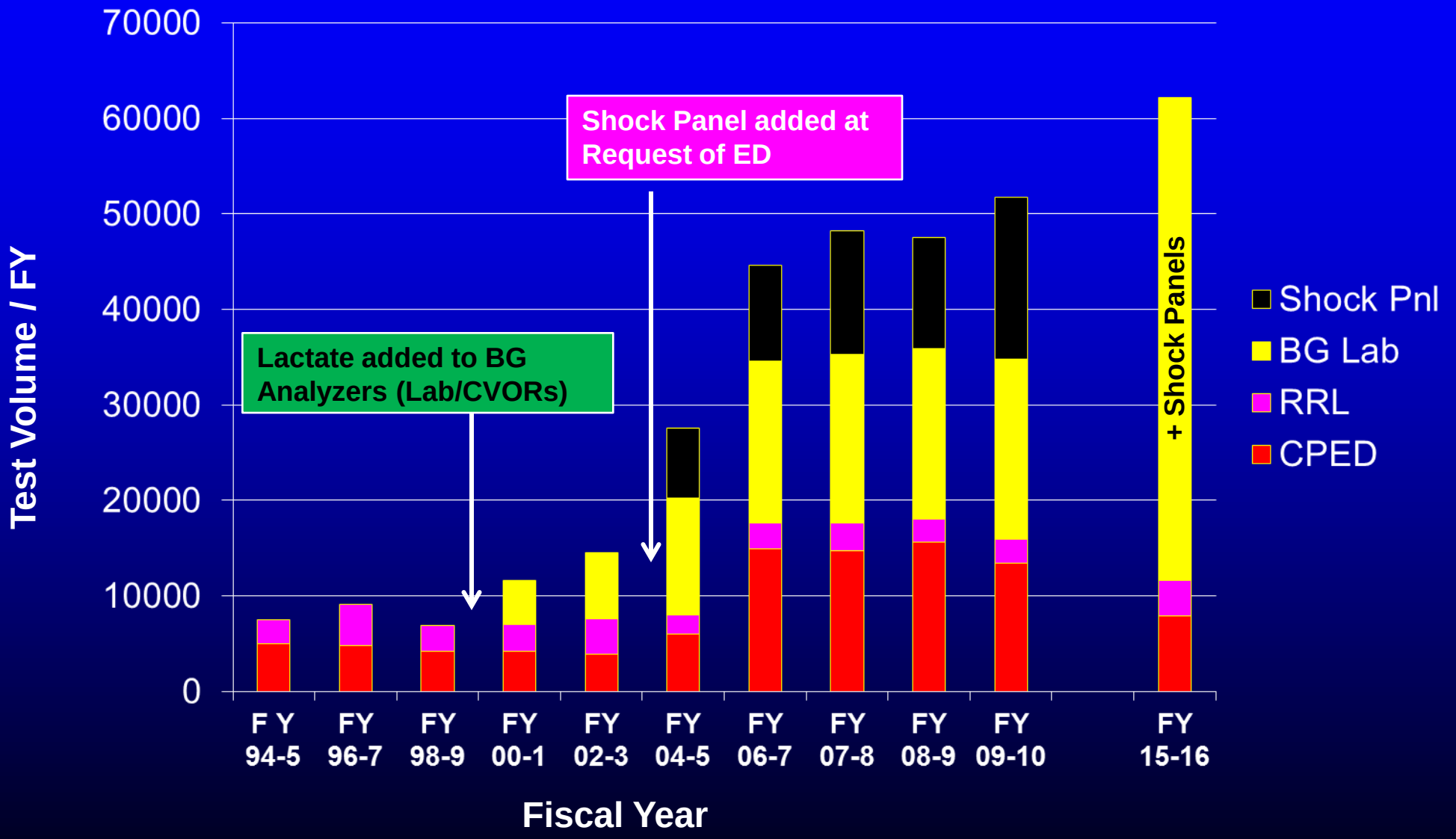
- There are several mechanisms that elevate lactate.
- Recommendation to monitor lactate testing in EGDT has markedly increased test usage.
- Lactate is becoming a marker for overall mitochondrial damage.
- When to measure and how to interpret?
  - Well established for peds open-heart, ECMO, sepsis, triage in ED.
  - Increased usage in adult open-heart surgery.

Potential Areas for POC or Lab Measurements of Lactate

Location	TA-Time Needed	POC	Near Pt Lab	Central Lab
Emergency Dept.	< 30 min	ED very chaotic (variable by hospital)	YES ($)	May be acceptable
Open-Heart Surgery	5-15 min	YES	YES ($)	NO
ECMO	5-30 min	YES (but low test #'s)	YES ($)	May be acceptable
Sepsis	60 min	YES (but many areas to cover)	YES ($)	May be acceptable

($) = Other tests and test volumes necessary to justify a near-patient laboratory.

Lactate Testing at Duke Medical Center



Thank you for your attendance and attention!