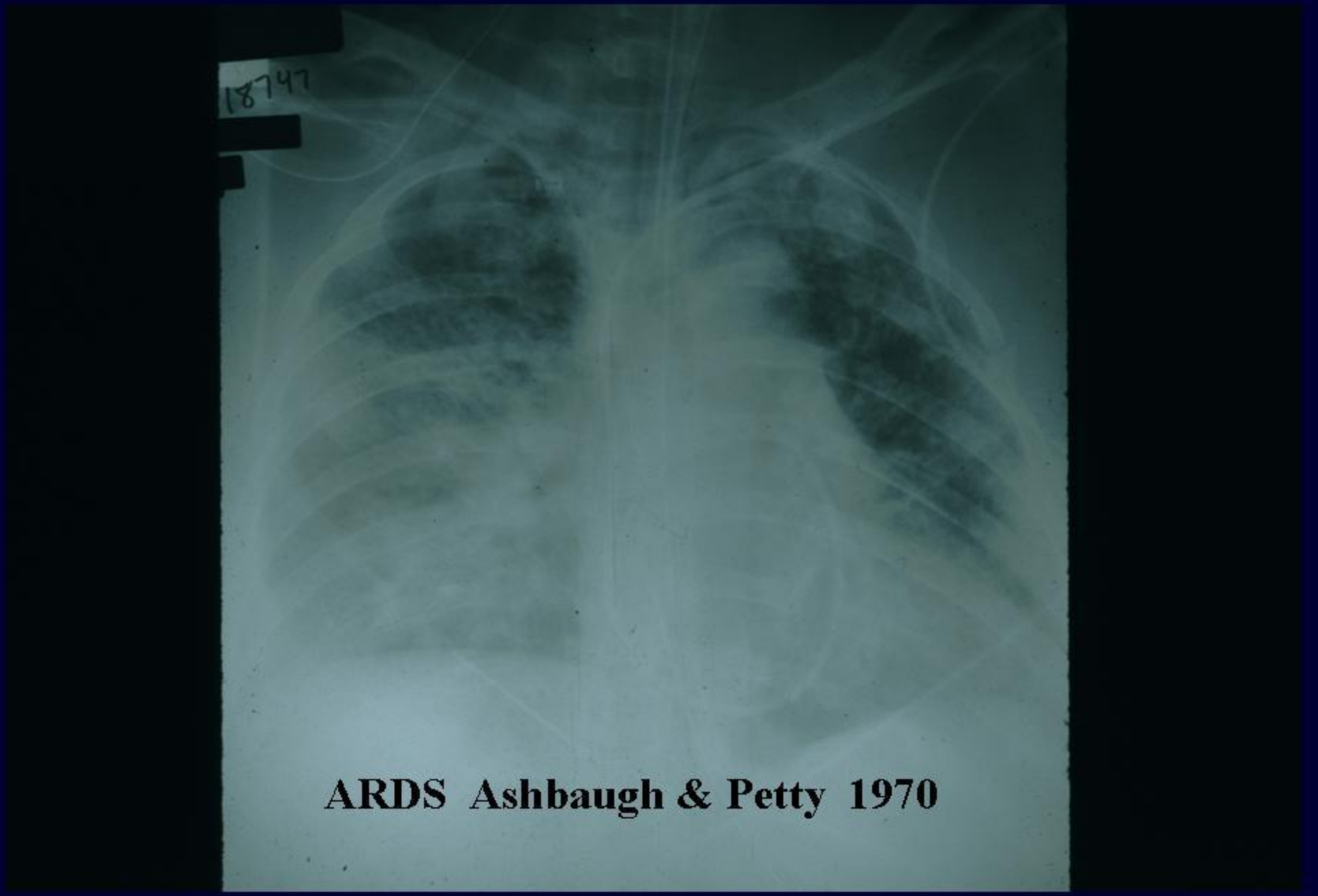
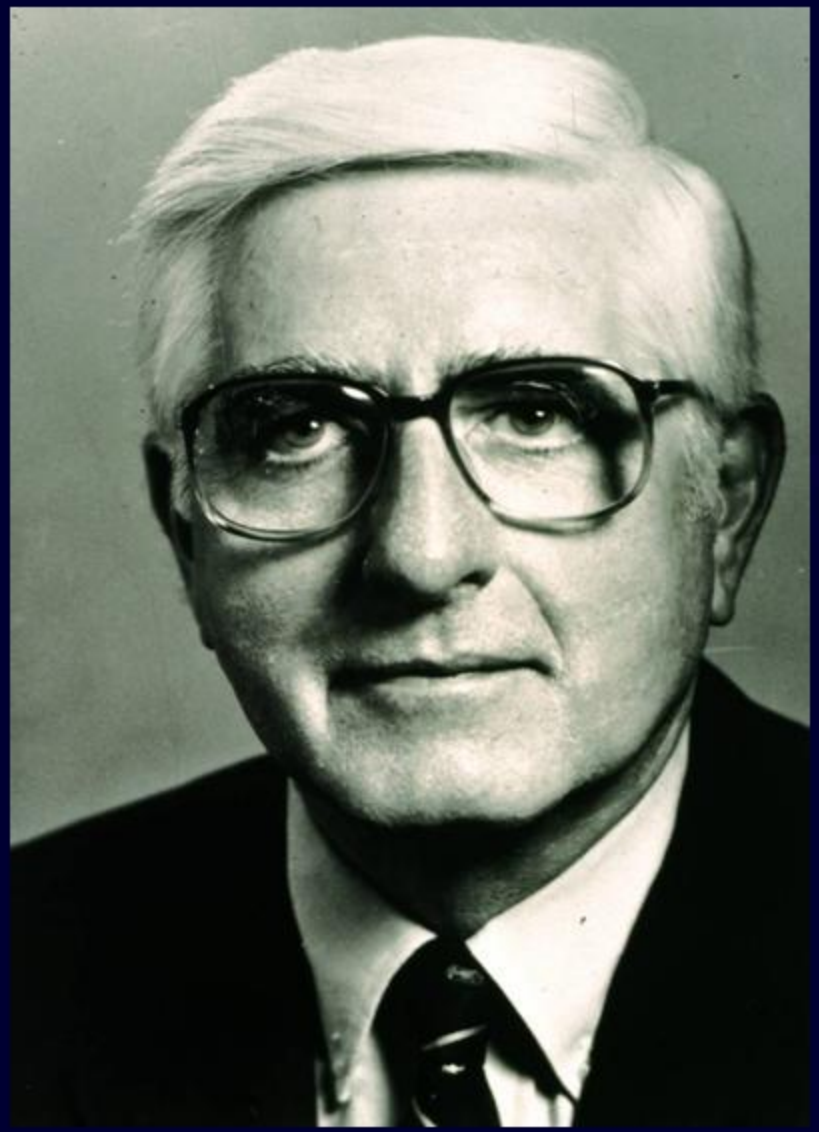
Postinjury Multiple Organ Failure

A/Prof. Zsolt Balogh, MD, PhD, FRACS
Director of Trauma
John Hunter Hospital
Newcastle
AUSTRALIA


18747
ARDS Ashbaugh & Petty 1970

Arthur Baue



EDITORIAL

MULTIPLE, PROGRESSIVE OR SEQUENTIAL SYSTEMS FAILURE
A Syndrome of the 1970's

Arch Surg 1975

MULTIPLE ORGAN FAILURE

Ben Eiseman

42 ICU Patients at Denver General

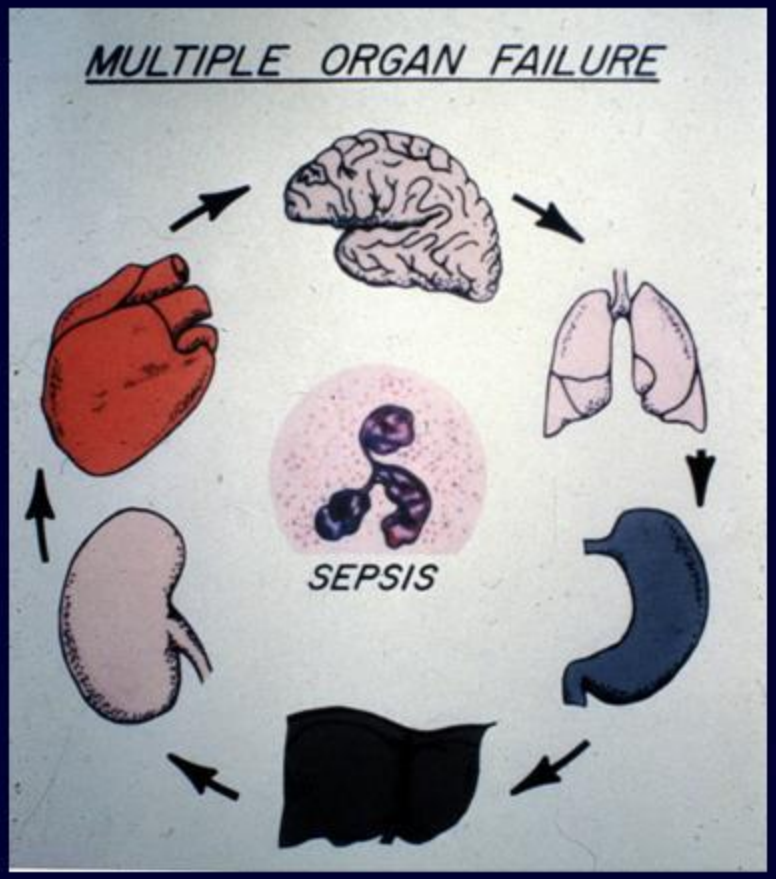
- Big Hit → Resuscitate
- Tranquil Period for Several Days
- Pathologic "Domino-Effect" of MOF

Risk Factors

- Pre - Existing Disease
- Shock
- Sepsis

SGO 1977

MOF OCCURS AS A RESULT OF UNCONTROLLED INFECTION



USA "Knife and Gun Clubs"

Abdominal Infection (50%)

Eiseman *SGO* 1977

Polk *Surgery* 1977

Fry *Arch Surg* 1980

? MOF ⟶ " Blind Lap "

MOF IN POLYTRAUMA PATIENTS

Eugene Faist

J Trauma 1983

433 Trauma Patients from Munich

Multiple Injuries - 99% Blunt Mech

34 (8%) MOF → 19 (56%) Died

Early MOF

Massive Shock/Tissue Injury

Can Not Resuscitate

Late MOF

Shock/Tissue Injury

Resuscitated → ? MOF

Delayed Sepsis → MOF

MOF OCCURS AS A RESULT OF AUTODESTRUCTIVE INFLAMMATION

Jan Goris

Arch Surg 1985

92 "SEPTIC" MOF PATIENTS

55 Trauma
(All Blunt)

24 (44%)

37 Non-Trauma
(GI Problems)

7 (19%)

No Focus of Infection
Found at Autopsy

SYSTEMIC INFLAMMATORY RESPONSE

"SEPSIS SYNDROME"

BACTERIAL TRANSLOCATION

"Passage of Viable Bacteria Through the Intact Mucosa of the GI Tract to MLNs and Other Organs"

Edwin A. Deitch

J Trauma 1985

Important Factors
- Bacteria
- Physical Barrier
- Mucosal Immunity

Primary Insults → BT to MLNs
- Shock
- Burns
- Endotoxin

Pre-conditioners → Amplify BT To Liver Spleen & Systemic Blood
- Malnutrition
- Antibiotic
- Bowel Rest

Gut Bacterial Translocation via the Portal Vein: A Clinical Perspective with Major Torso Trauma *J Trauma, 1991*

FREDERICK A. MOORE, M.D., ERNEST E. MOORE, M.D., RENATO POGGETTI, M.D., OLIVER J. McANENA, M.D., VERLYN M. PETERSON, M.D., CHARLES M. ABERNATHY, M.D., AND POLLY E. PARSONS, M.D.

PORTAL VEIN SURVEILLANCE

20 Severely Injured Patients

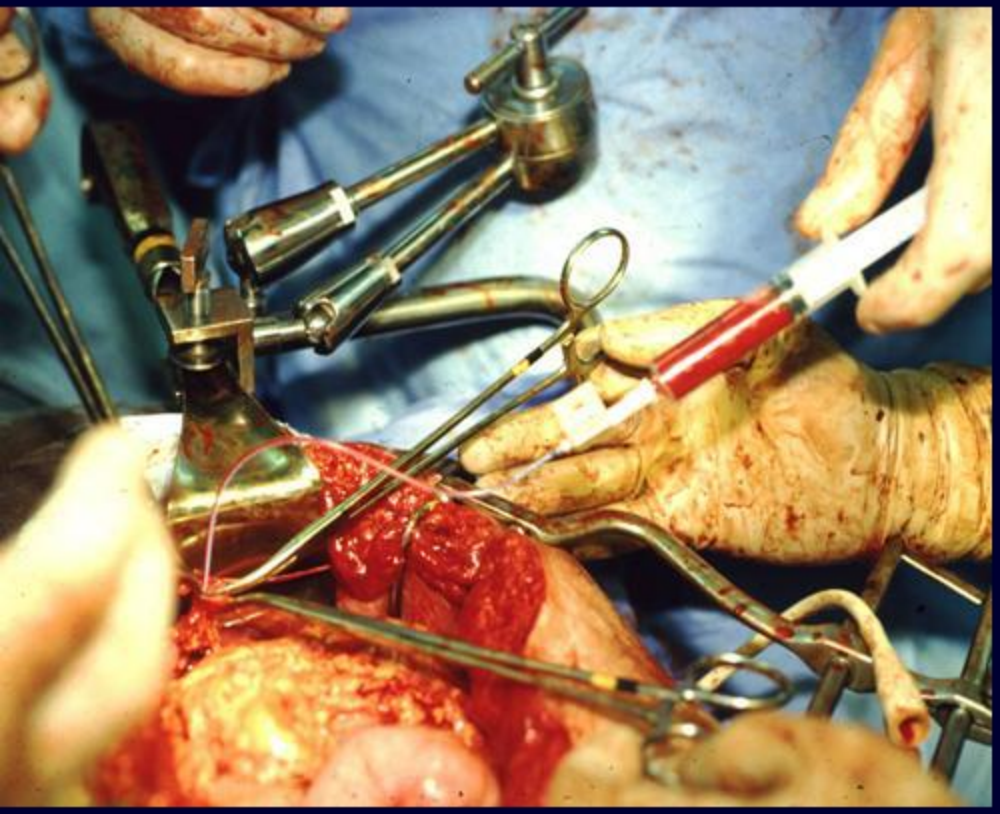
11 Massive Transfusions

6 Major Abdominal Trauma

3 Multiple Pelvic & Extremity Fractures

6 Developed MOF → 3 Died

PORTAL & SYSTEMIC BLOOD
Sampled at 0, 6, 12, 24, 48, 128 hrs



Blood Cultured

Blood Assayed

- Endotoxin
- Tumor Necrosis Factor
- Interleukin-6
- Complement C_{3a}

OUTLINE

- Definition
- The Problem
- History
- Epidemiology
- Predictors
- Prevention and Treatment strategy
- Future directions

BLOOD CULTURE RESULTS

Portal Cultures: 4% Positive

5 Coagulase Neg Staph

2 Propianibacterium Acnes

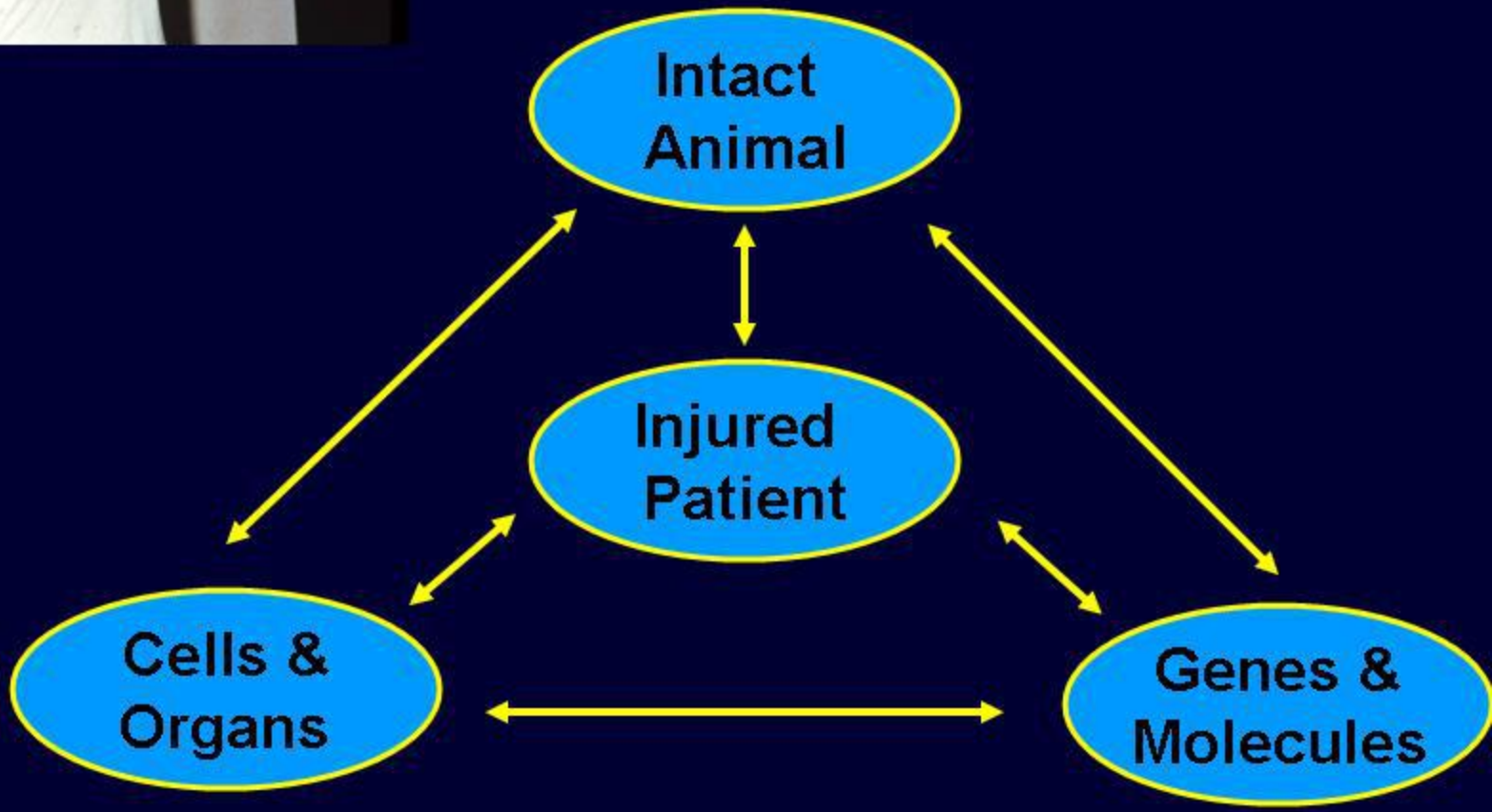
1 Acinobacter

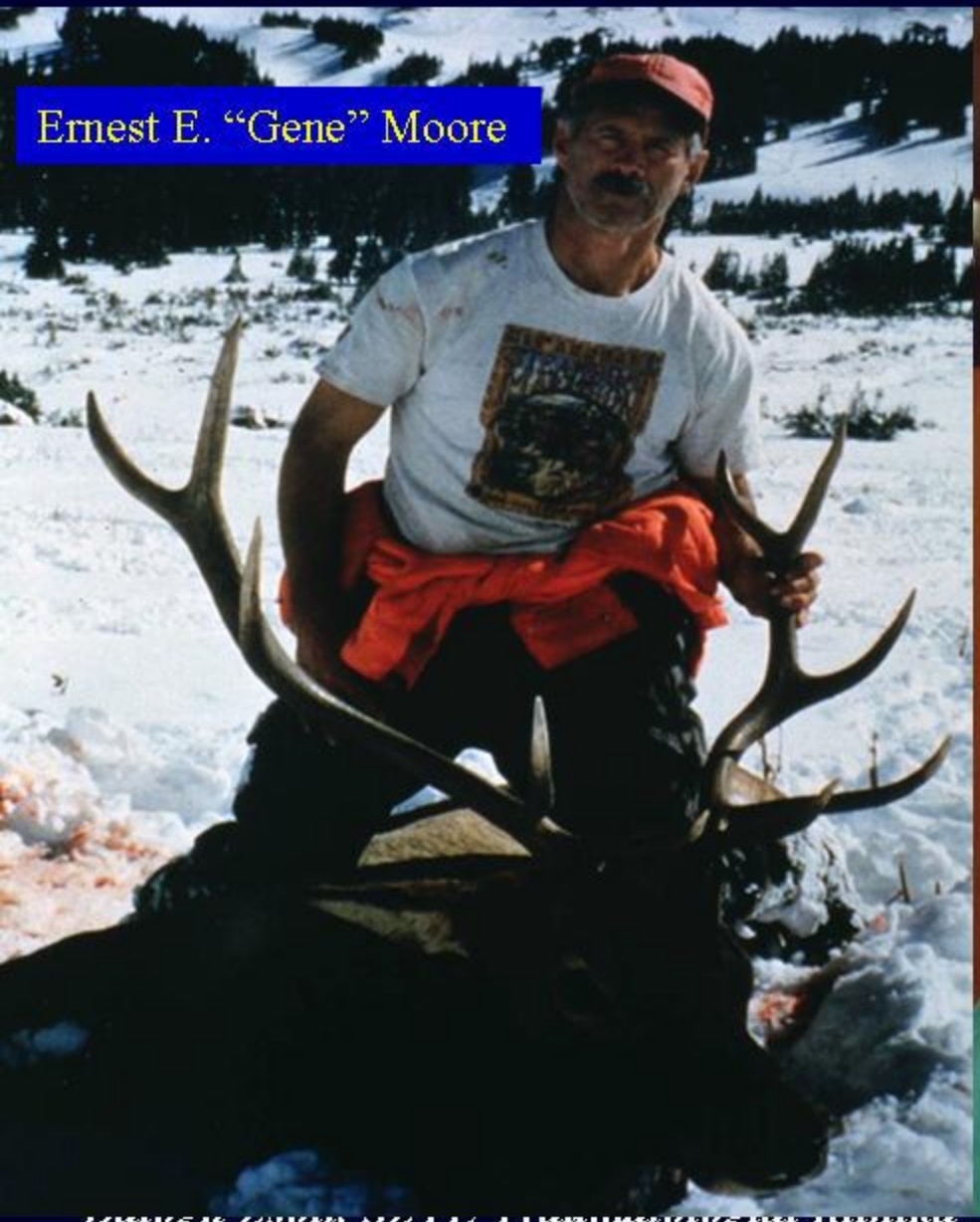
Systemic Cultures: 0.5% Positive

1 Staph. Aureus

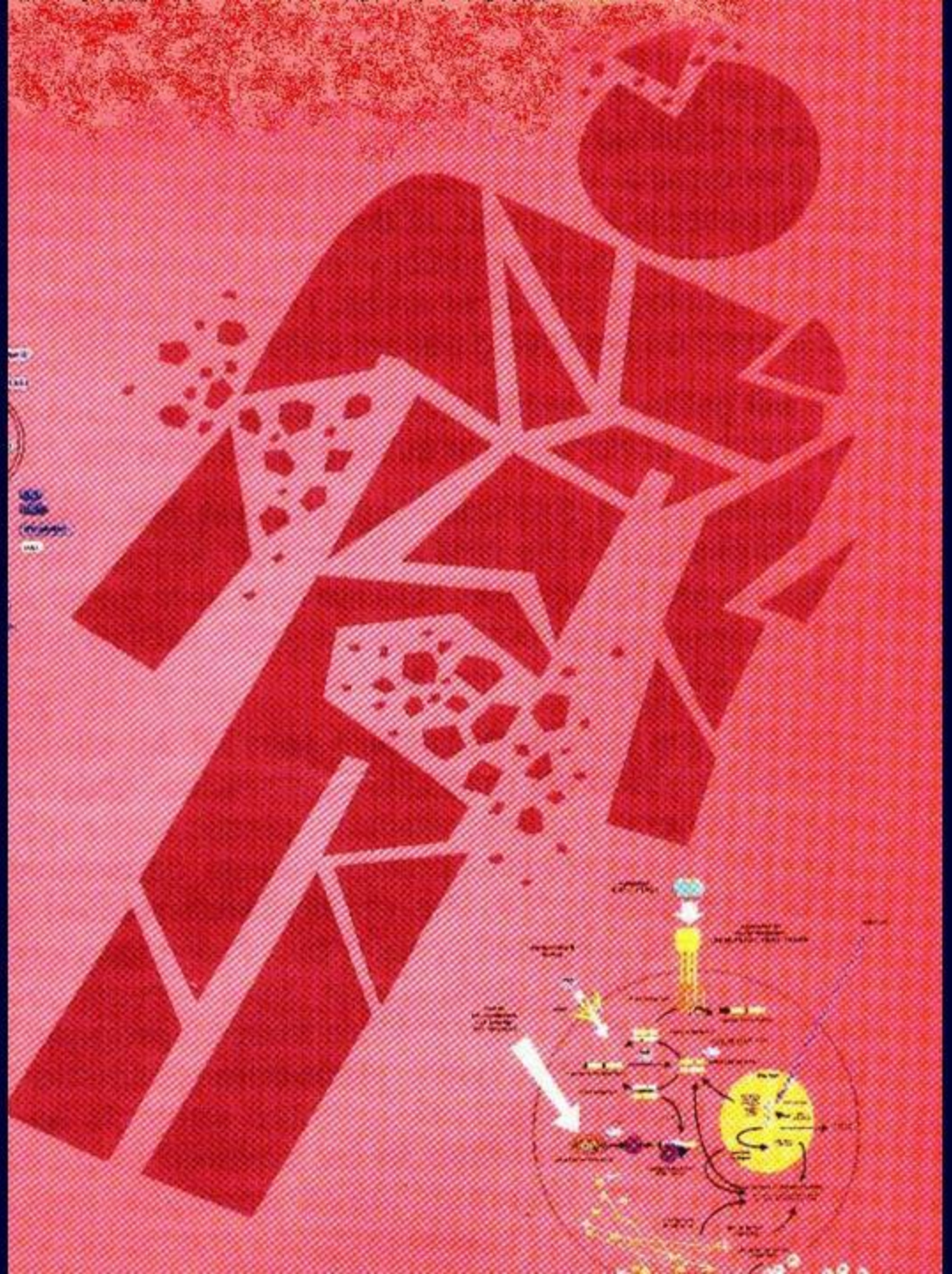
Alden Harkin

TRAUMA RESEARCH CENTER
UNIVERSITY OF COLORADO




Ernest E. “Gene” Moore


Frederick A. Moore

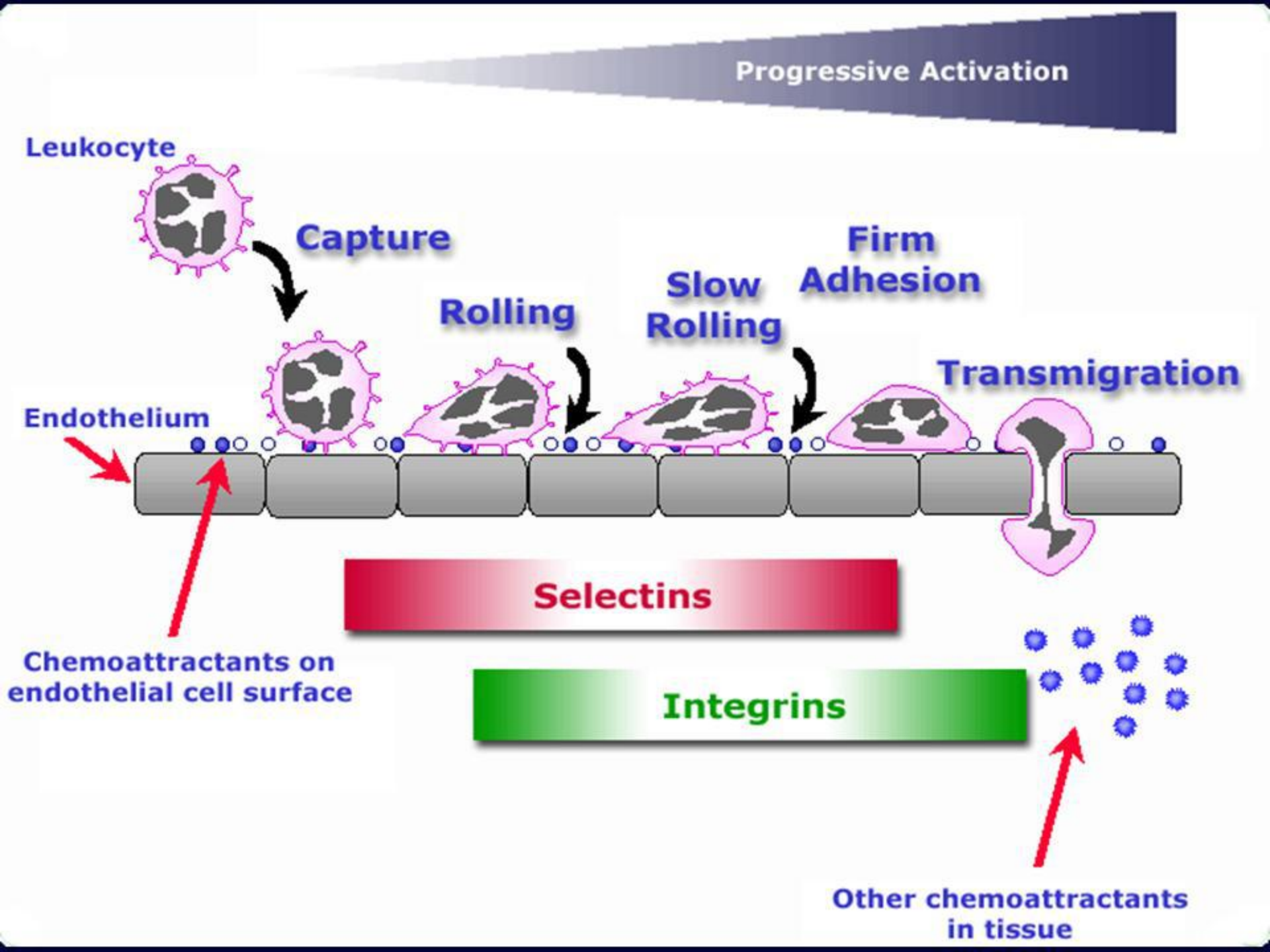


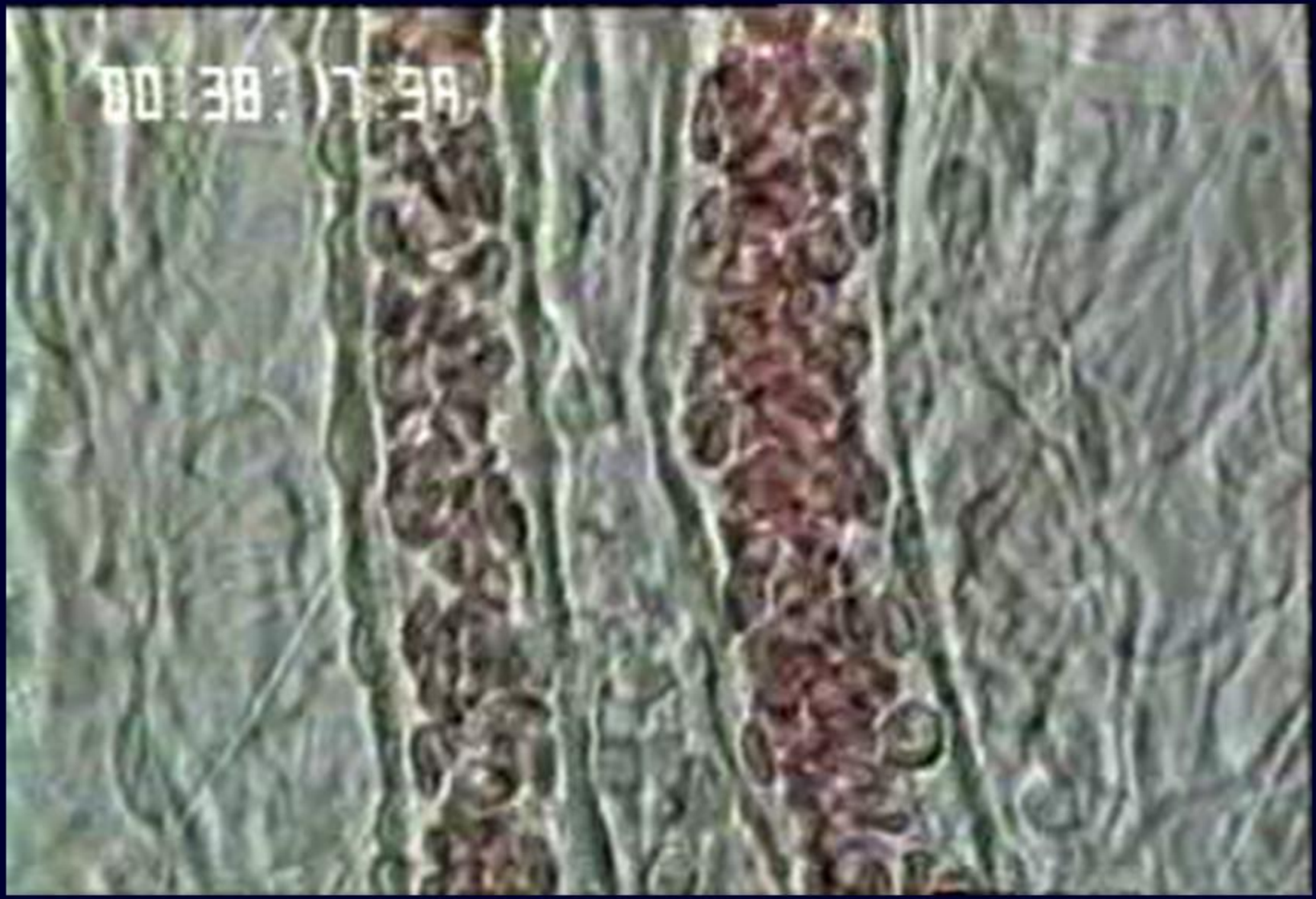
Tissue Injury

- Major
  - Enough itself to change homeostasis
- Minor
  - Not enough itself
  - Special injured area + physiologic response

Response to Major Trauma

- SHOCK phase: hypoperfusion, acute dysfunction
- RESUS phase: whole body I/R
- SIRS phase: hypermetabolic state
- MOF phase: result of over-activated and/or dysfunctional inflammation


Progressive Activation
Leukocyte
Capture
Rolling
Slow Rolling
Firm Adhesion
Transmigration
Endothelium
Selectins
Integrins
Chemoattractants on endothelial cell surface
Other chemoattractants in tissue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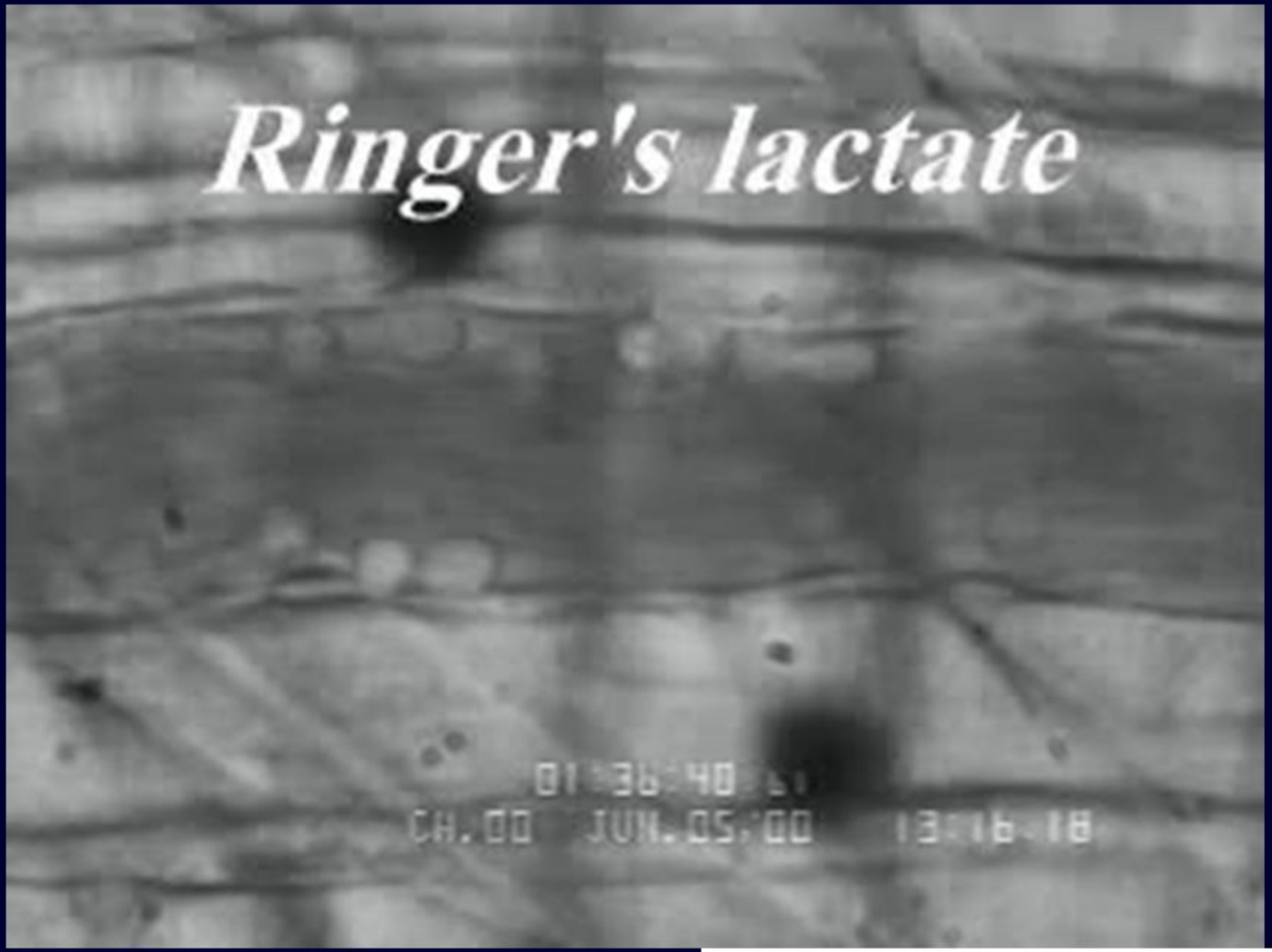


Balogh et al J Trauma 2002

Balogh et al J Trauma 2002

Denver MOF Scale*

	Grade 0	Grade 1	Grade 2	Grade 3
A. Pulmonary** $Pa O_2/Fi O_2$	P/F > 250	P/F 250-175	P/F 175-100	P/F < 100
B. Renal	Normal Cr < 160	Cr > 160	Cr > 220	Cr > 450
C. Hepatic	Normal T Bili <35	T Bili > 35	T Bili > 70	T Bili >140
D. Cardiac	No Inotropes	Minimal Inotropes (<5)	Moderate Inotropes (5-15)	High Inotropes (>15)

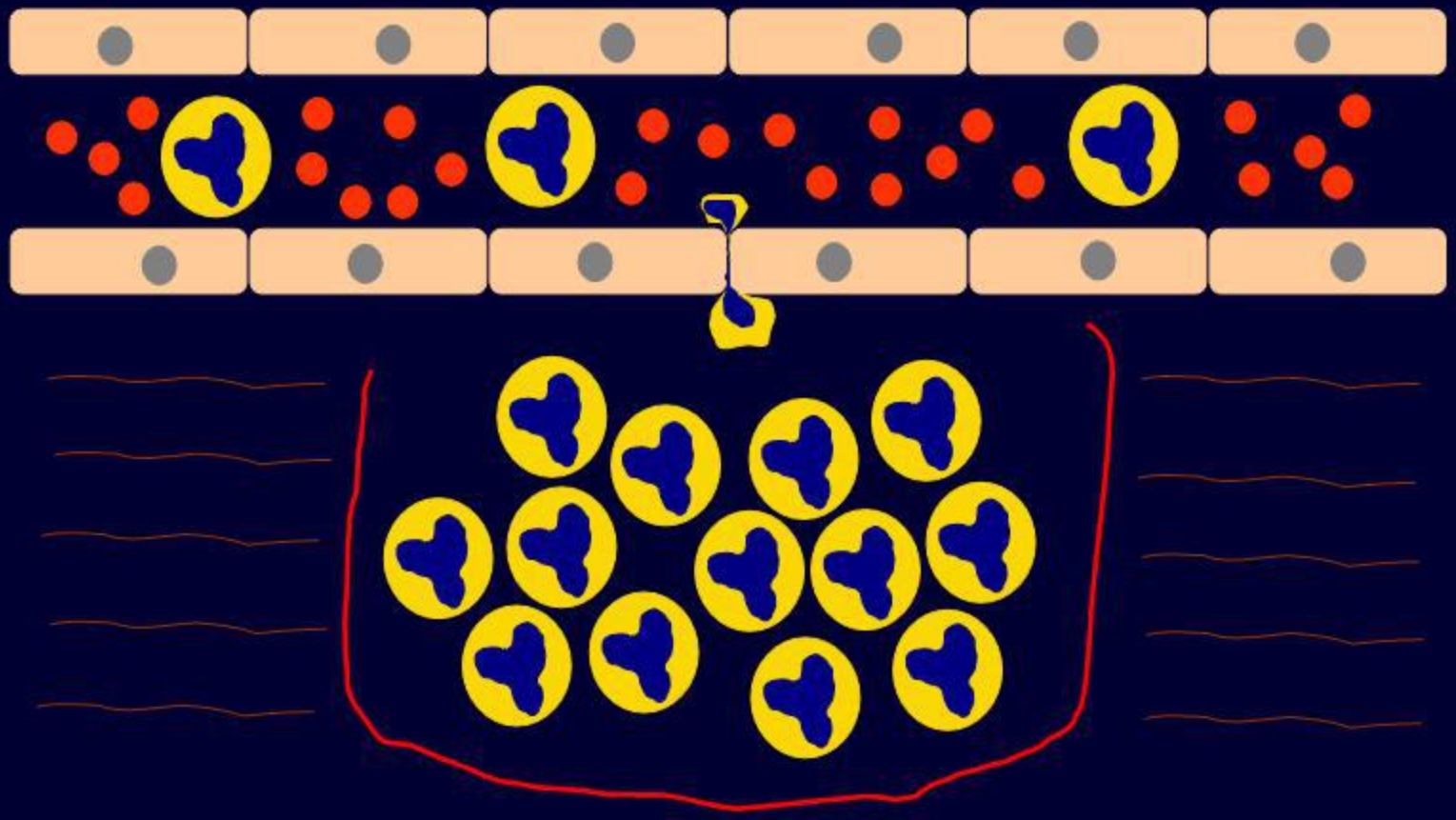
Organ Failure Score = A+B+C+D

MOF = Score > 3

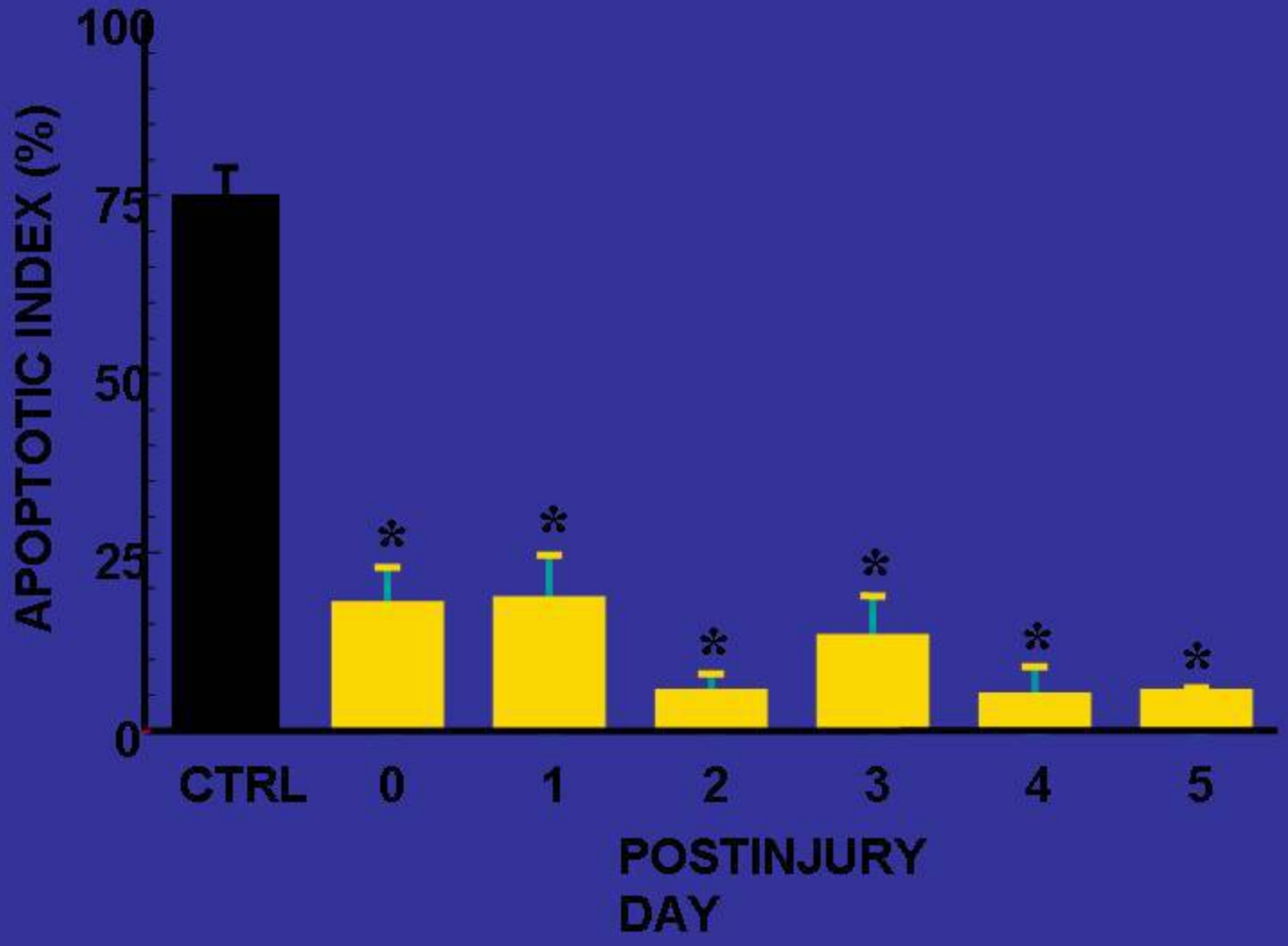
*Moore, Moore, Poggetti, *J Trauma* 31:629 (1991)

**Offner, Moore,, *J Trauma* 55:285 (2003)

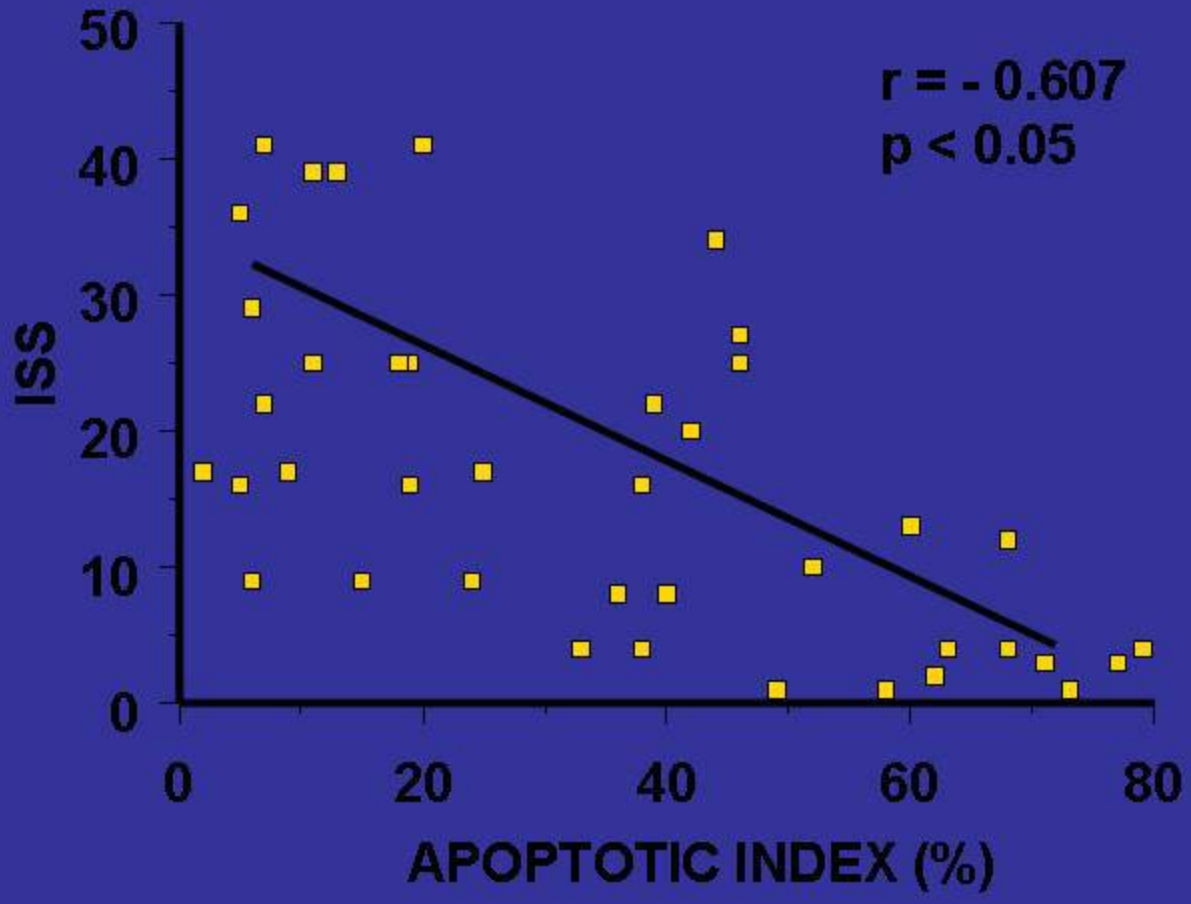
PMN SEQUESTRATION



POSTINJURY PMN APOPTOSIS



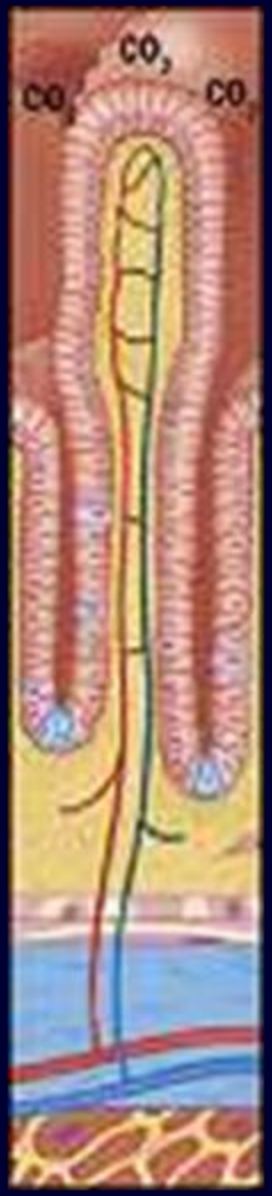
PMN APOPTOSIS AND INJURY SEVERITY



HIGH RISK PATIENTS

Index	Apoptotic
MOF	8 ± 1
No MOF	27 ± 6

Apoptotic Index Independently Predictive of MOF (p=.08)



GASTRIC REGIONAL PCO_2

PrCO2 (mmHg)

70
60
50
40
30

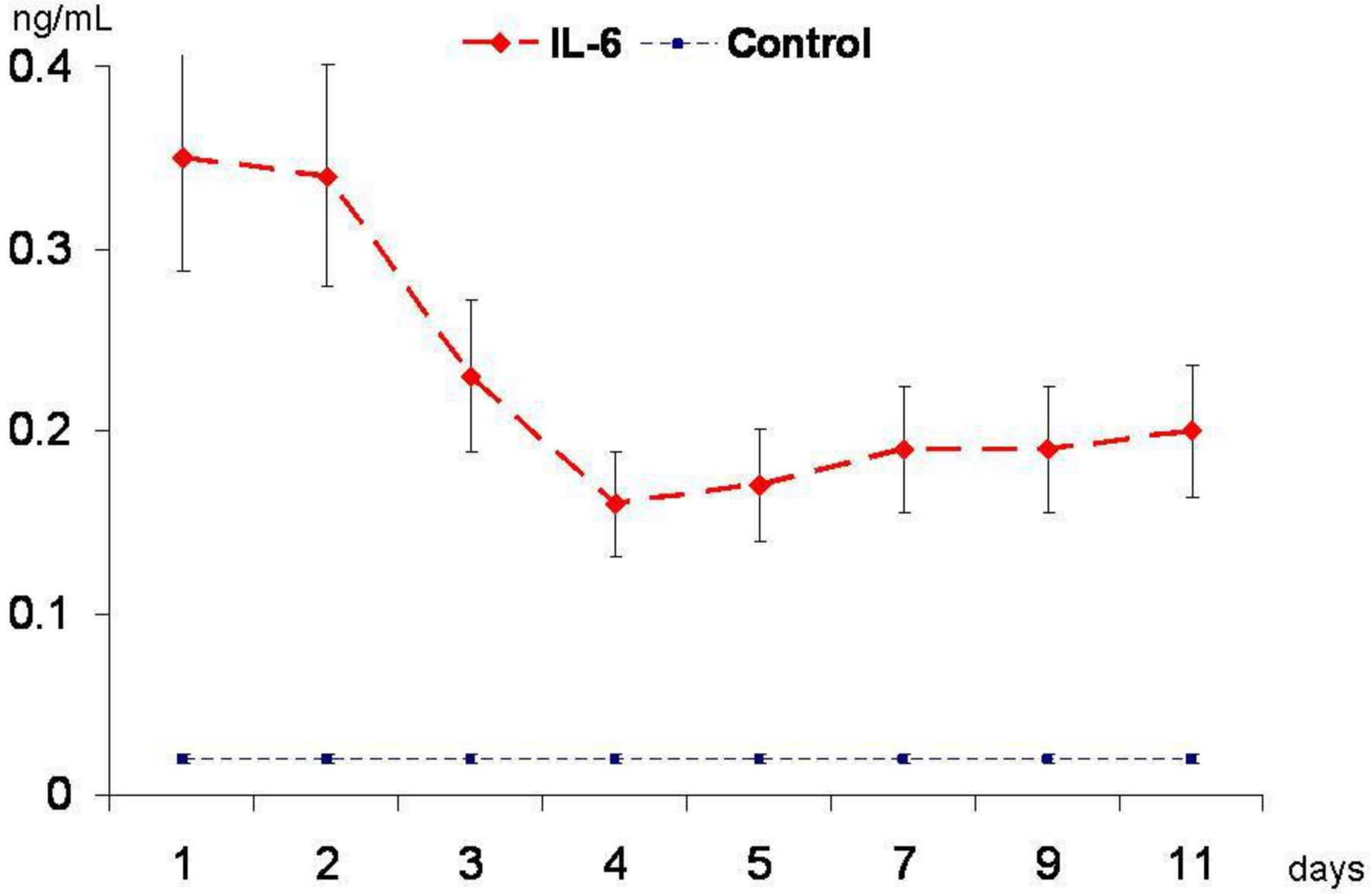
0 4 8 12 16 20 24 28 32 36

TIME (hr)

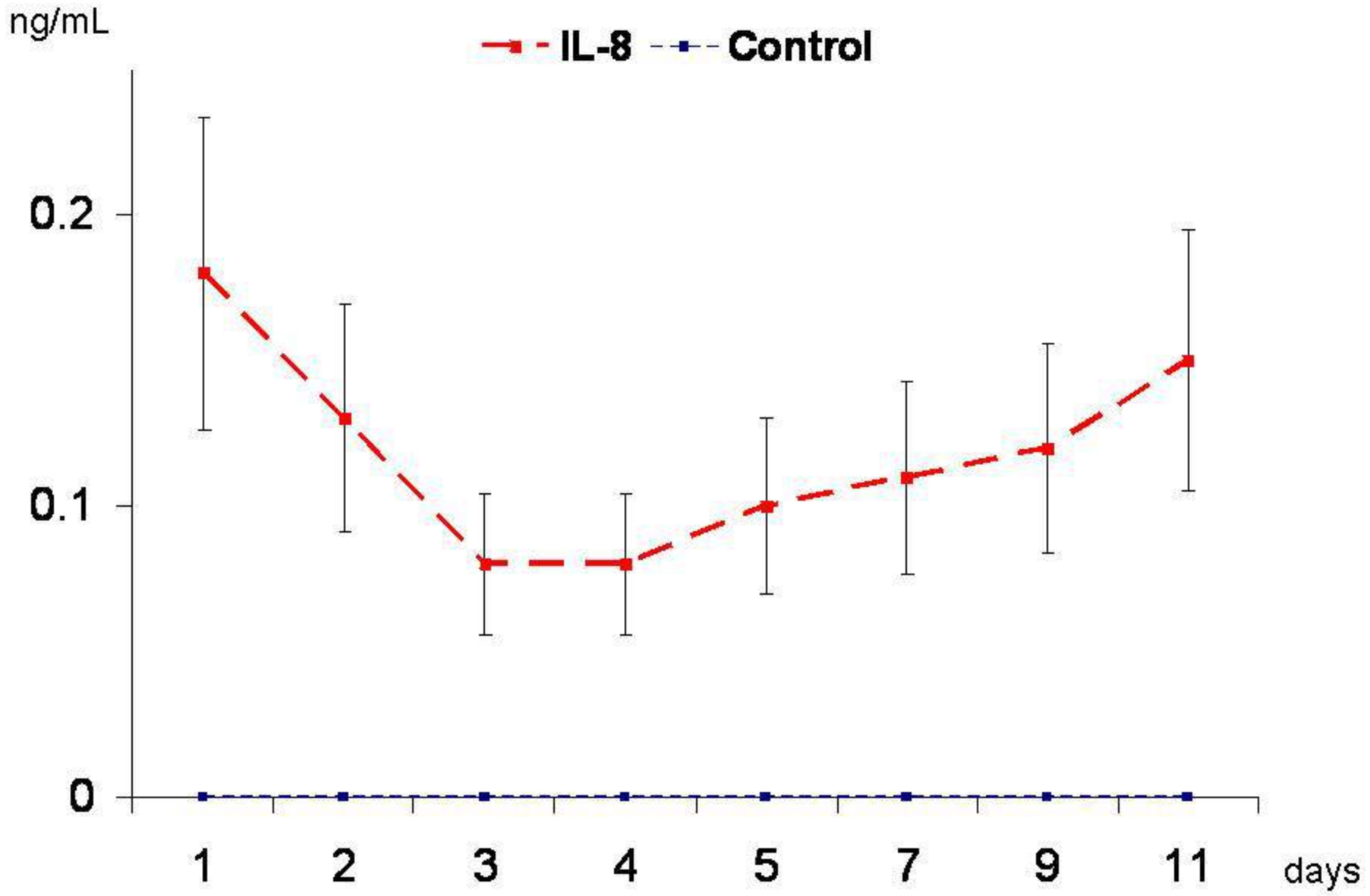
ARDS/MOF (N=12)

NO ARDS/MOF (N=22)

Polytrauma Patients' Inflammatory Markers 1-11 days from Injury

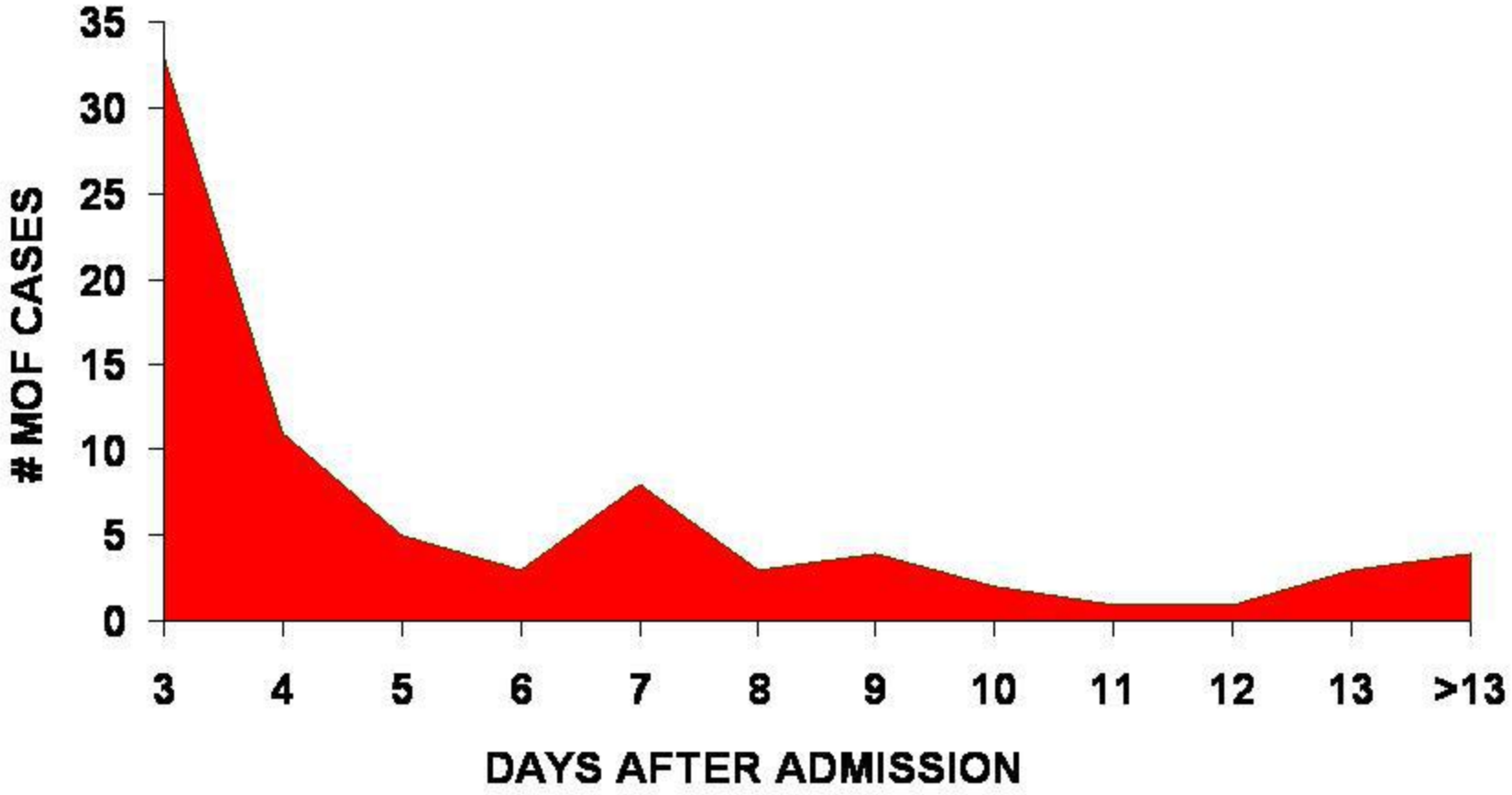


Polytrauma Patients' Inflammatory Markers 1-11 days from Injury

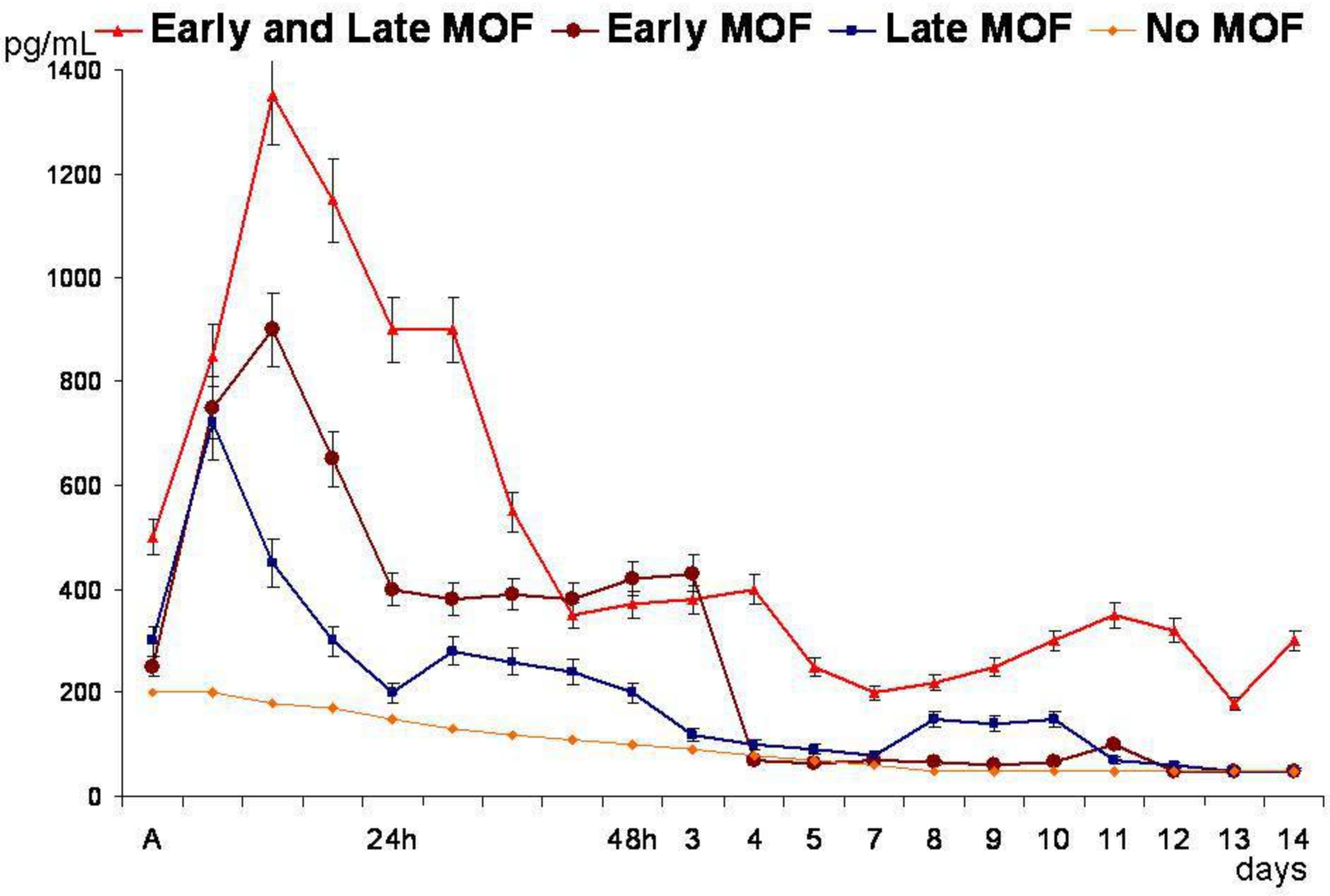


	MOF + death	OF / MOF	No MOF
No. patients	11	38	17
ISS	43	42	35
Age	45	39	34
SBP<90	36%	34%	6%
U of Blood	9	8	4
Vent days	20	24	6
Worst PO_2/FiO_2	134	181	289
ICU LOS	20	31	11
Lactate	4.8	5.0	3.1
A-III % of norm	49	48	62
Elastase	221	217	117
IL-6 (12 hours)	1969	703	177
IL-8 (12 hours)	1602	1101	301

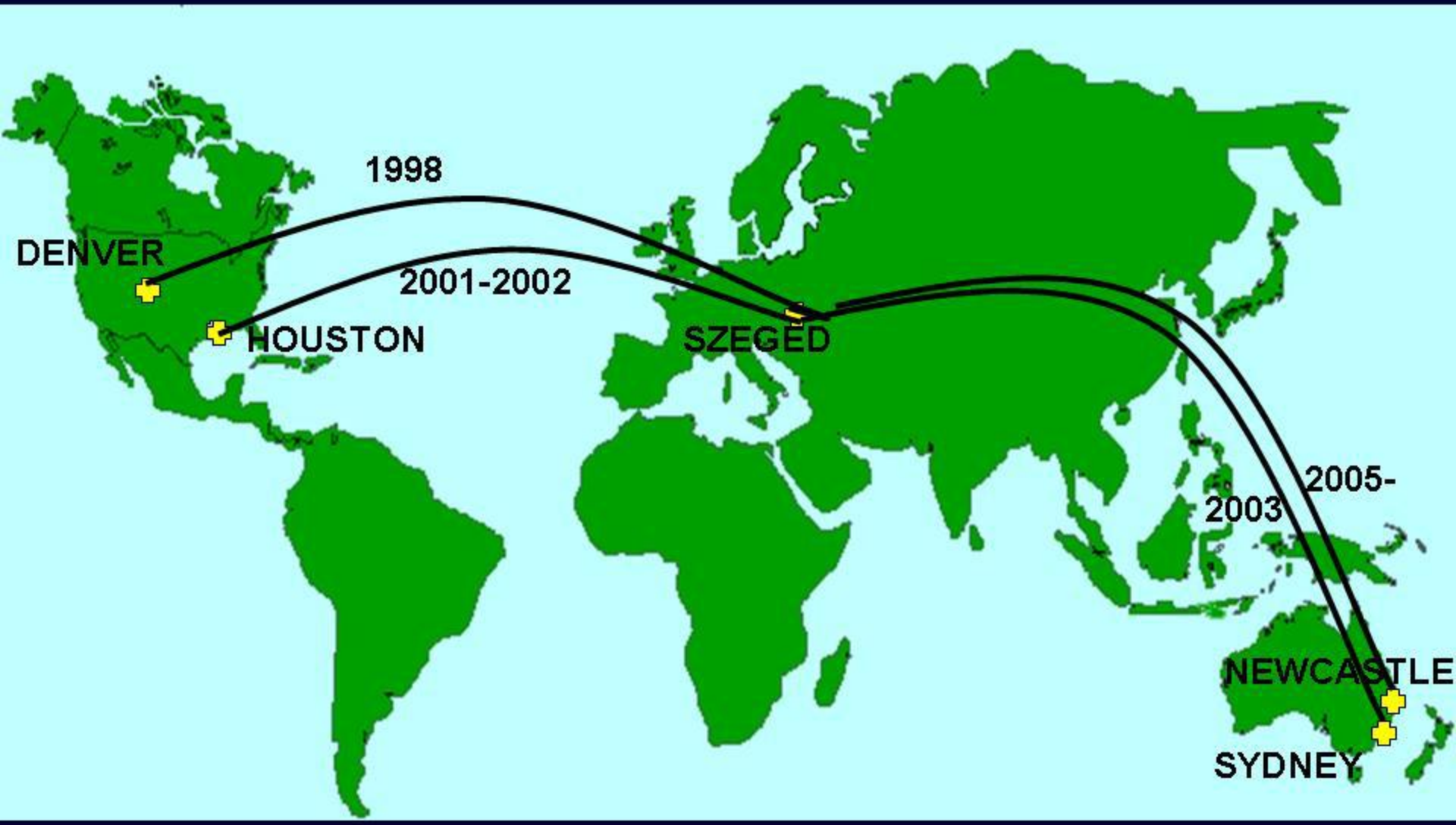
Time Pattern of Post-Injury MOF



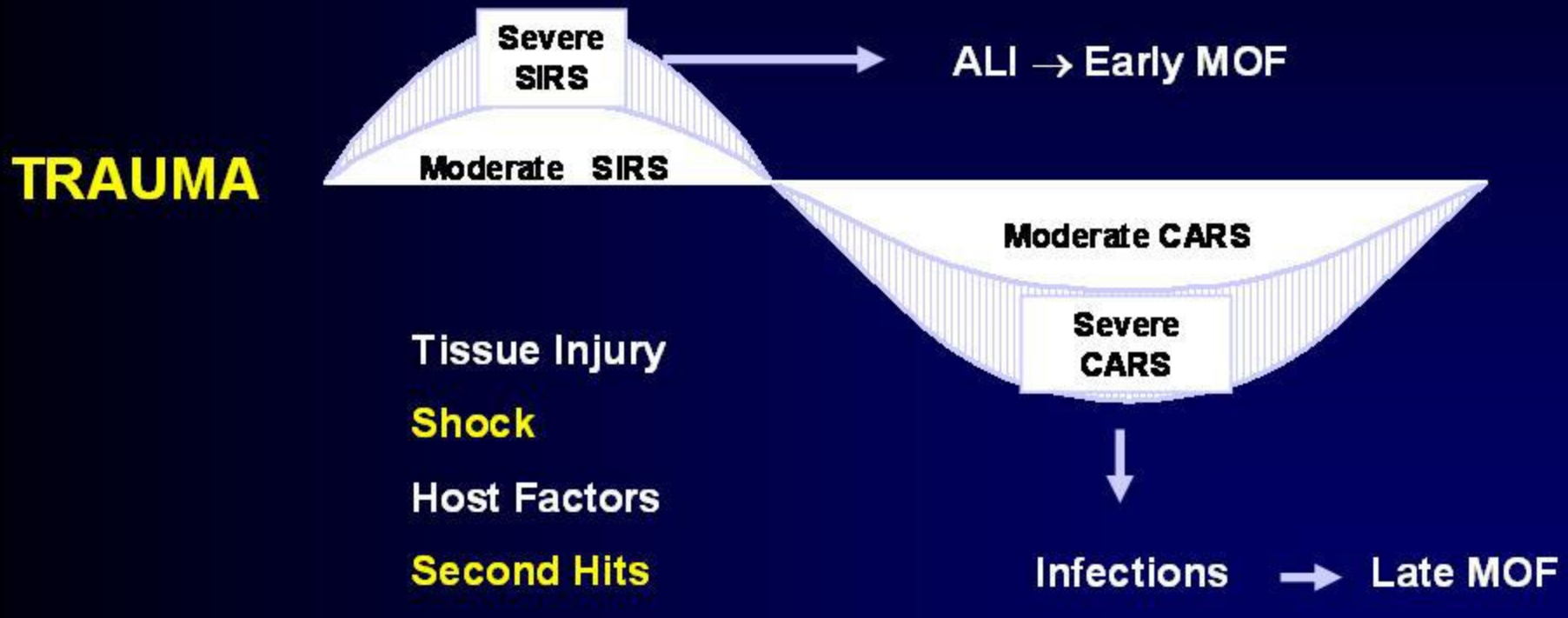
Polytrauma Patients' IL-6 Concentration



TRAUMA-SHOCK-ACS-MOF



POSTINJURY MOF OCCURS AS A RESULT OF A DYSFUNCTIONAL INFLAMMATORY RESPONSE



Bimodal Phenomenon

1. Refractory Shock
2. SIRS $\rightarrow$ Early MOF
3. Infections $\rightarrow$ Late MOF

Multiple Organ Failure Can Be Predicted as Early as 12 Hours after Injury

J Trauma 1998

Angela Sauaia, MD, PhD, Frederick A. Moore, MD, Ernest E. Moore, MD, Jill M. Norris, PhD, Dennis C. Lezotte, PhD, and Richard F. Hamman, MD, DrPH

ACUTE PREDICTION MODELS

Host Factors

- Age > 55 years

Tissue Injury

- ISS > 25

Shock Indices

- Blood Transfusion > 6 units
- ED Base Deficit > 8mEq/L
- Lactate > 2.5 mmol/L after 12 hrs of resuscitation

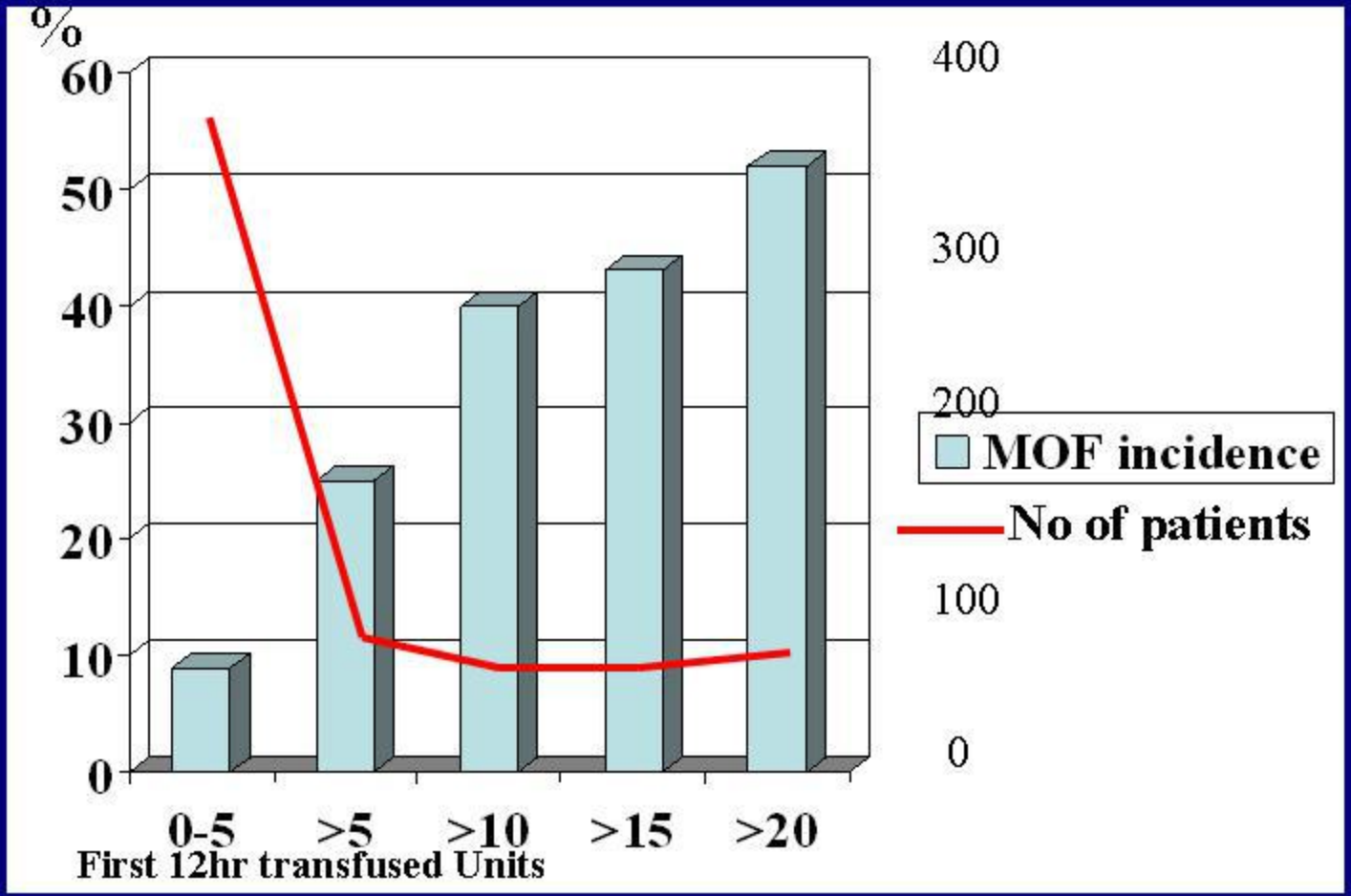
Second Hits

SECOND HITS

- Bad timing
- Transfusions
- Operations
- Diagnostics
- Transfusions
- Infections
- Complications

THE AGE OF THE TRANSFUSED BLOOD AND MOF

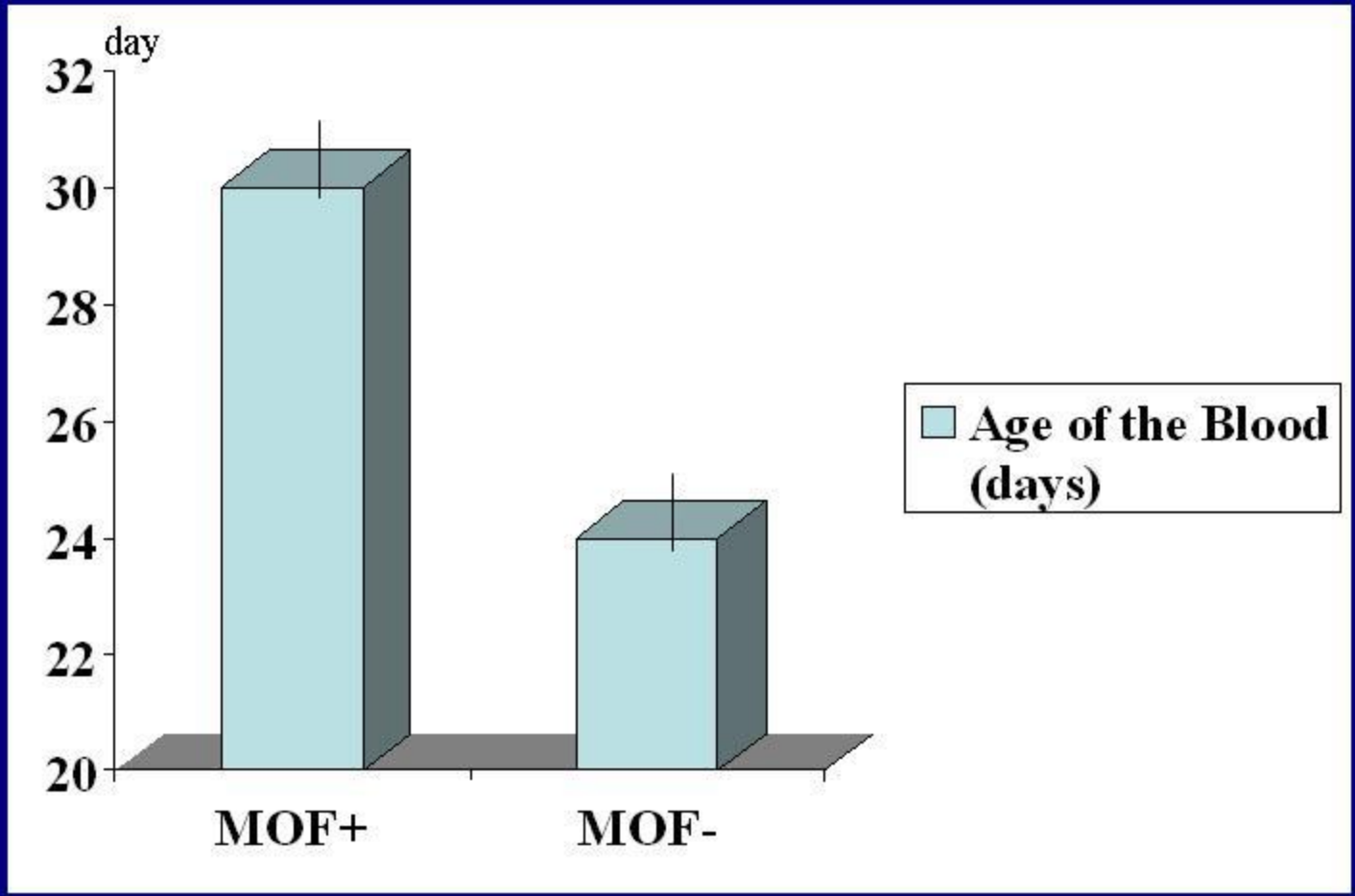
N= 513
MOF= 85



N= 513

MOF= 85

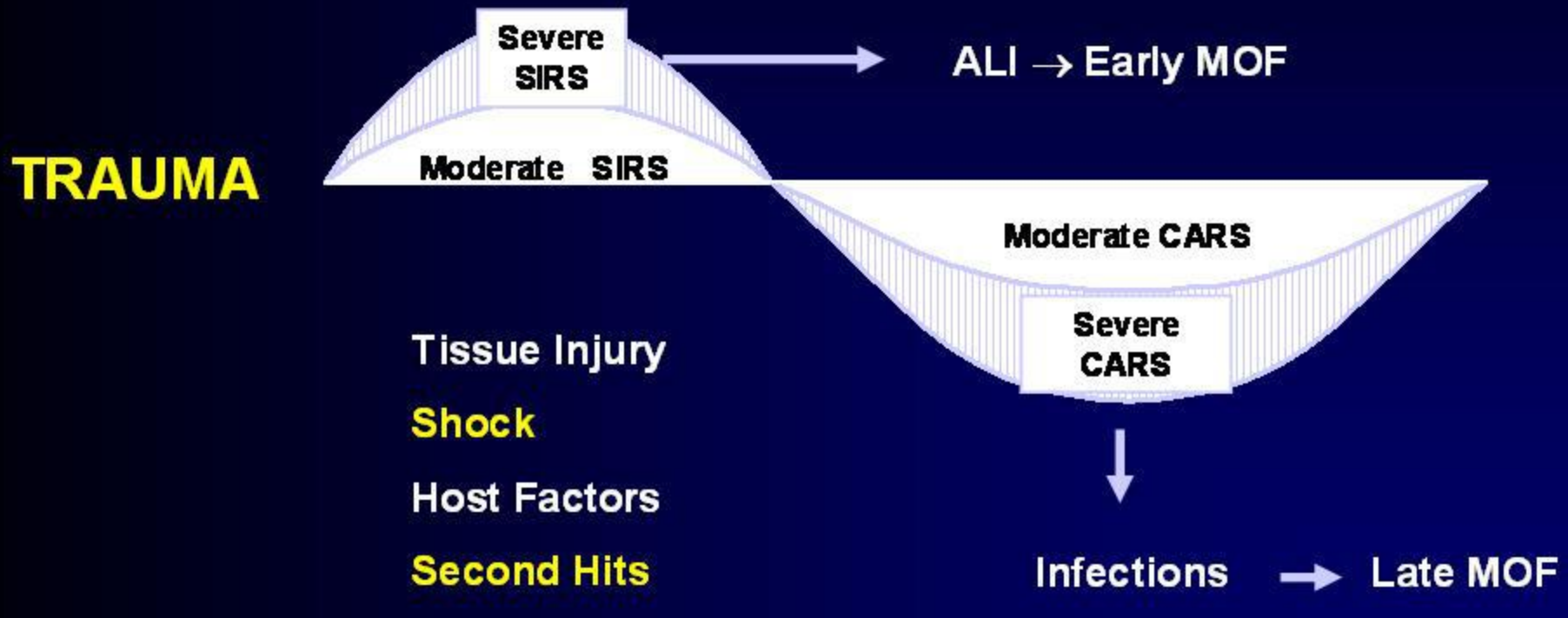
Age of the blood ~ MOF risk

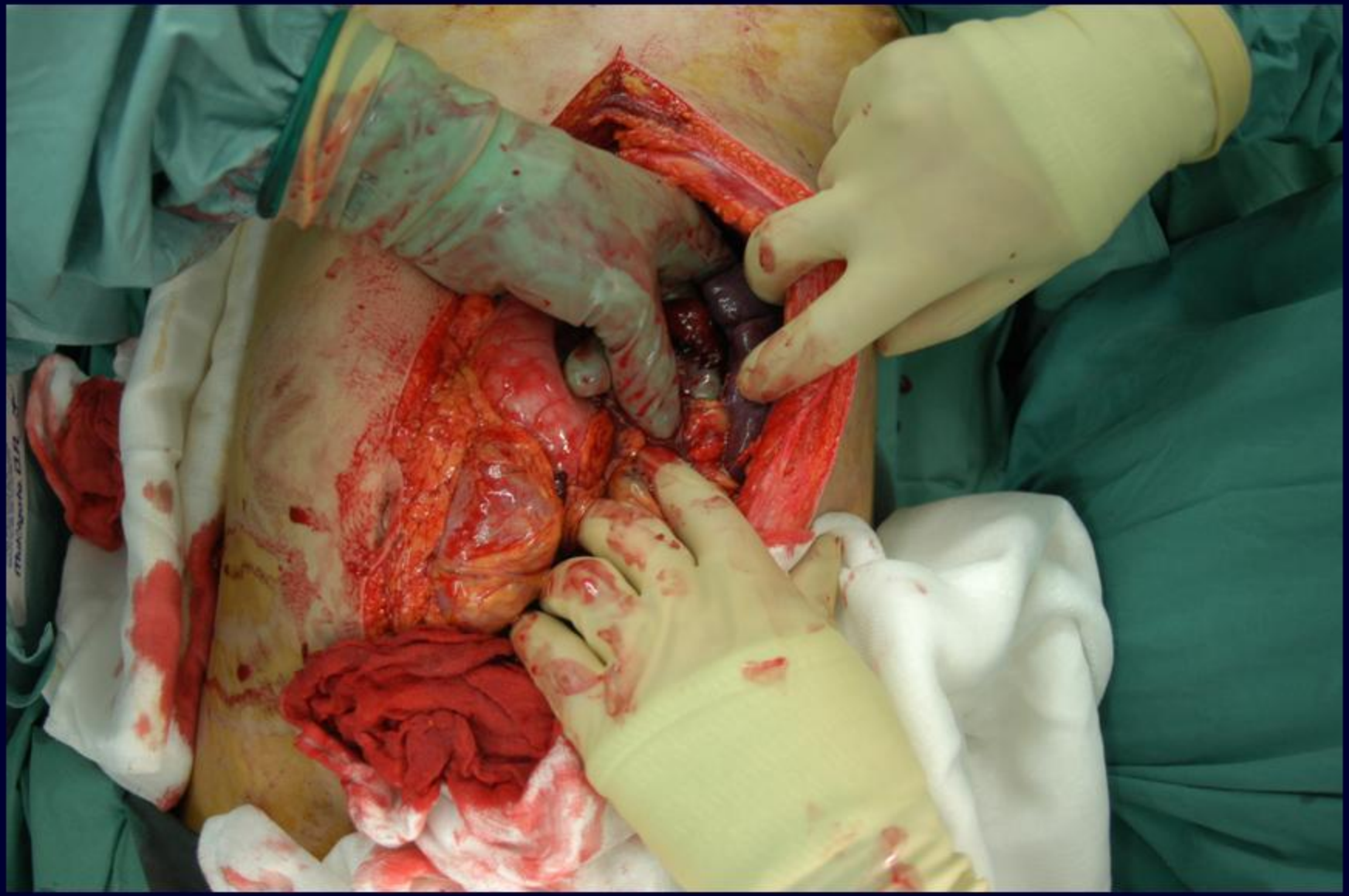


MTT 2001

SZTE TRAUMATOLÓGIA

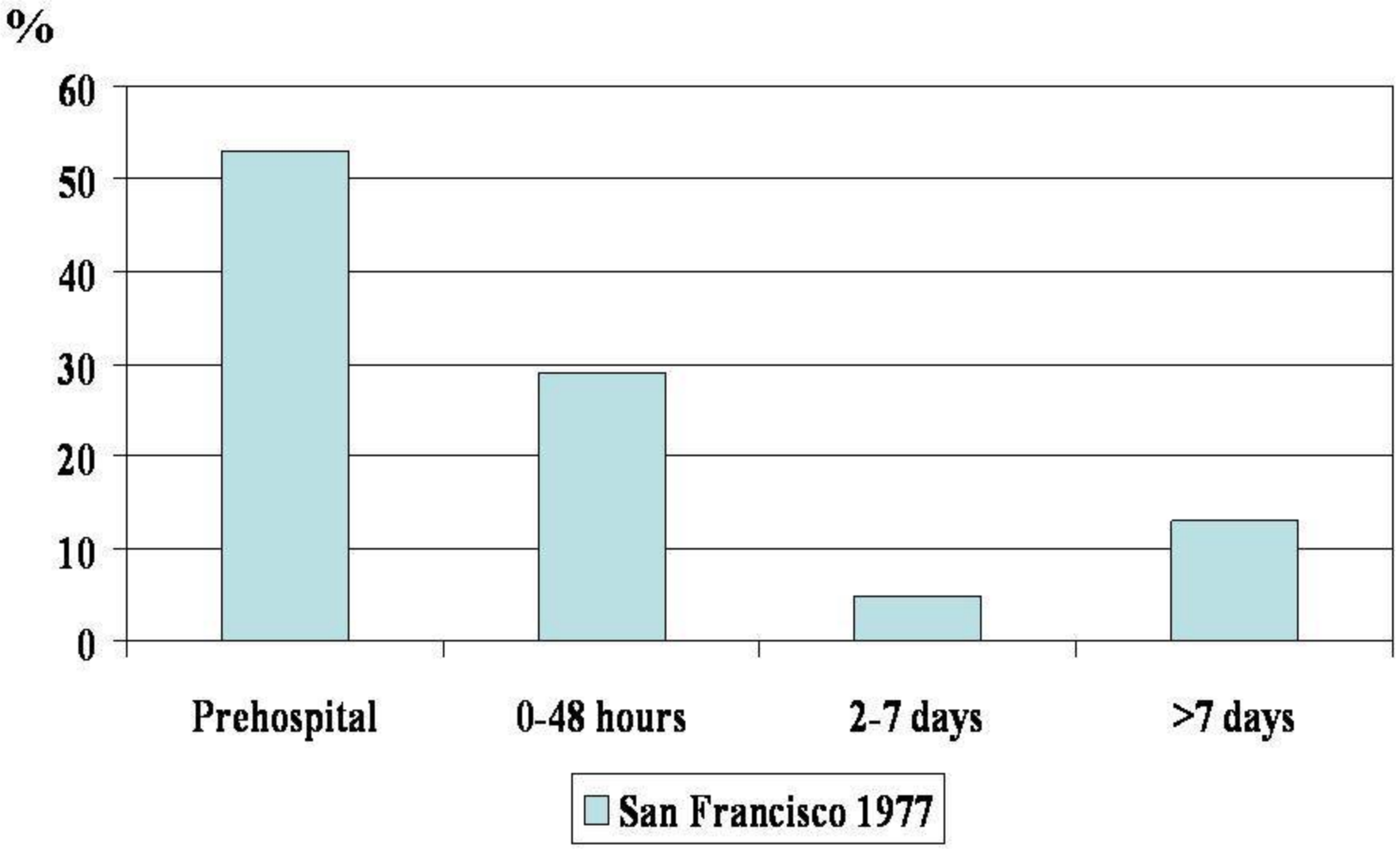
POSTINJURY MOF OCCURS AS A RESULT OF A DYSFUNCTIONAL INFLAMMATORY RESPONSE

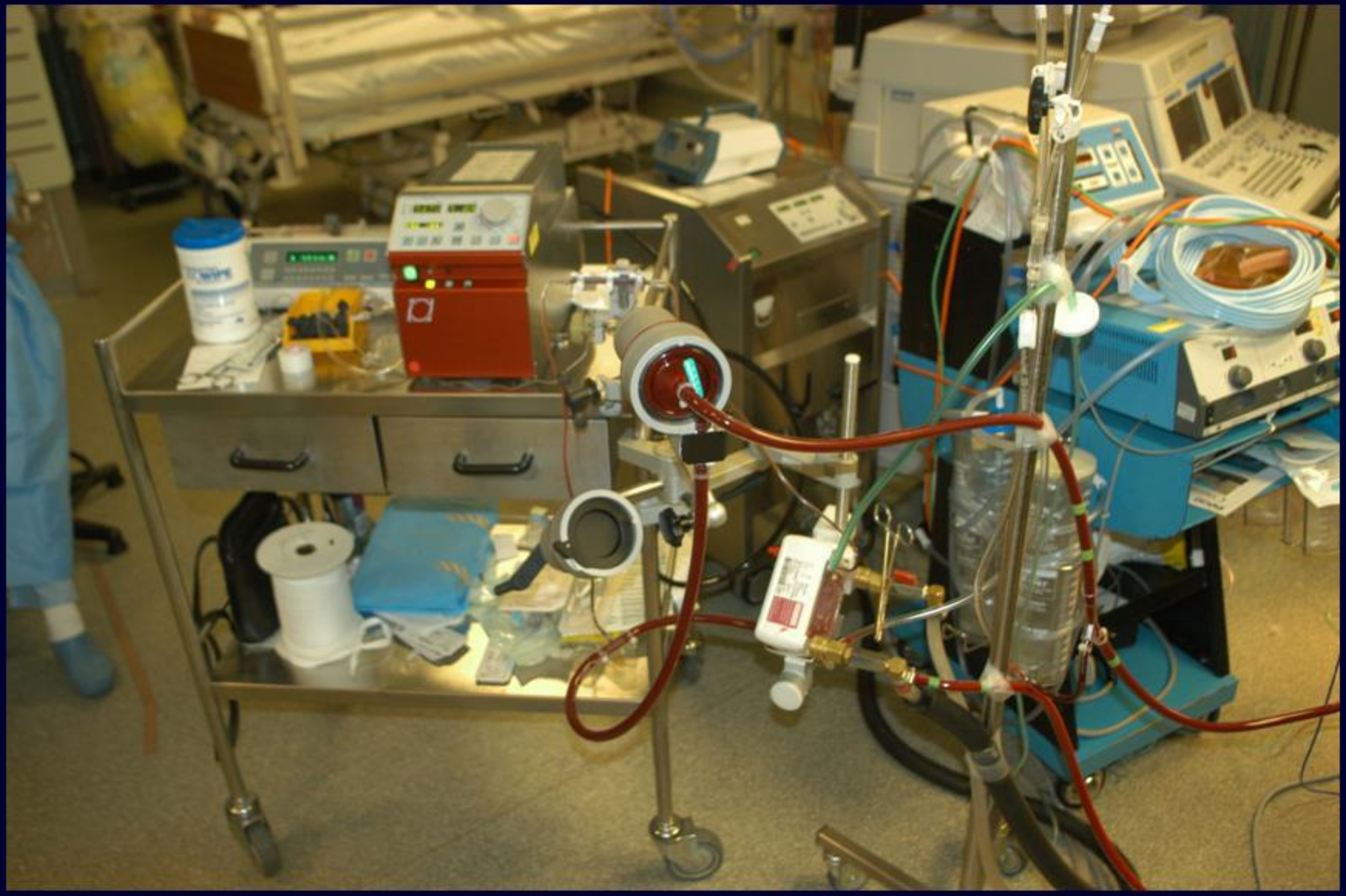


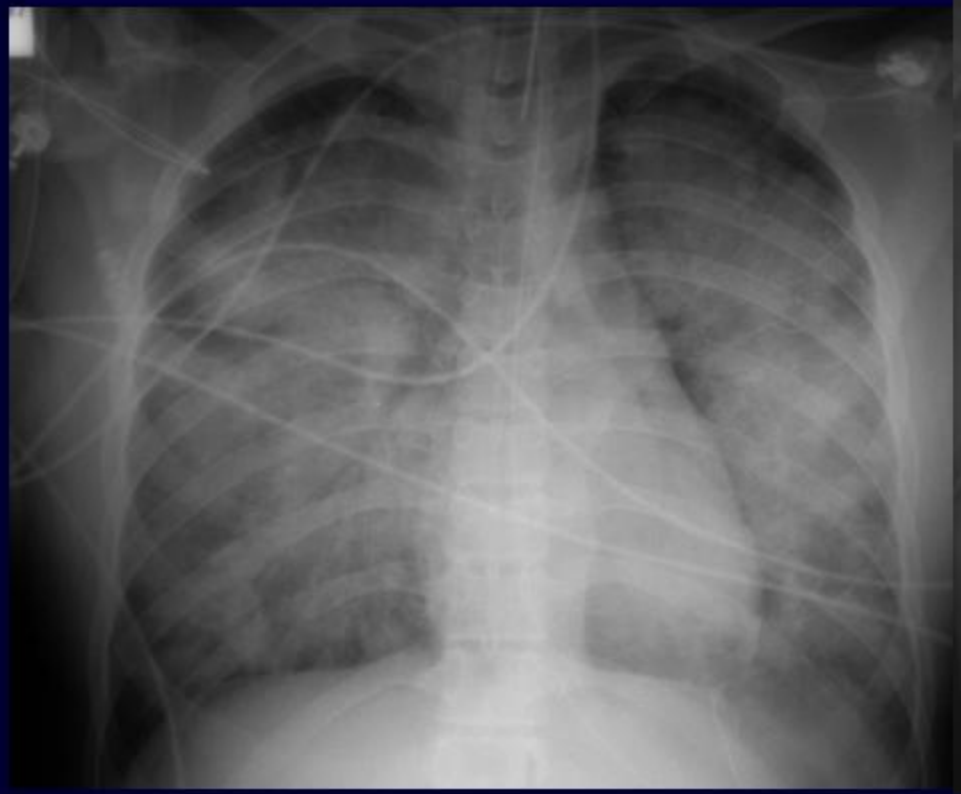


Trauma Deaths (%)

john hunter trauma service







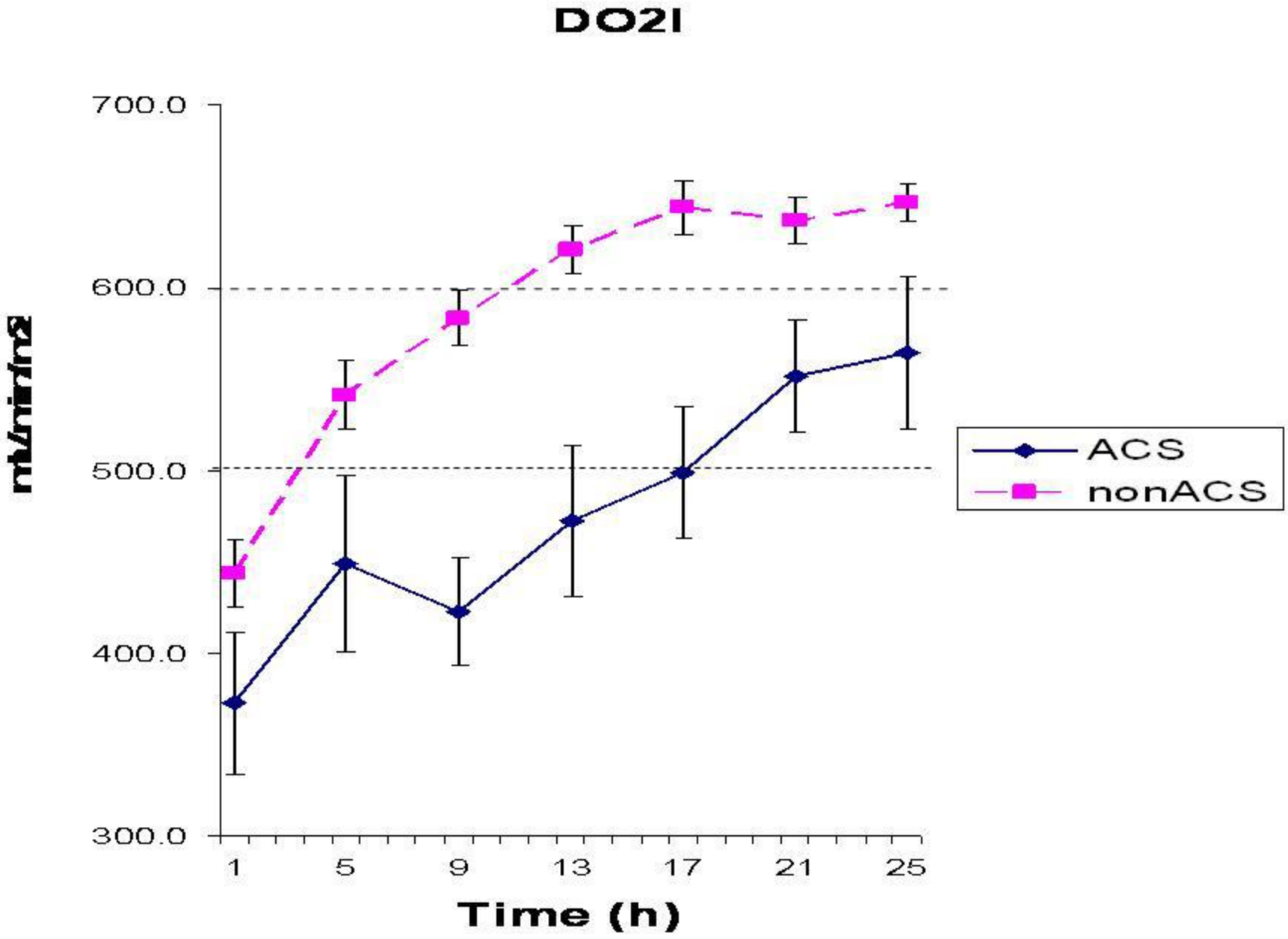
O.K. But what to do with the patient?

1. Is the patient high risk for MOF?
2. Does the patient have massive immune response?
3. Is the patient high-risk for second hits?

O.K. But what to do with the patient?

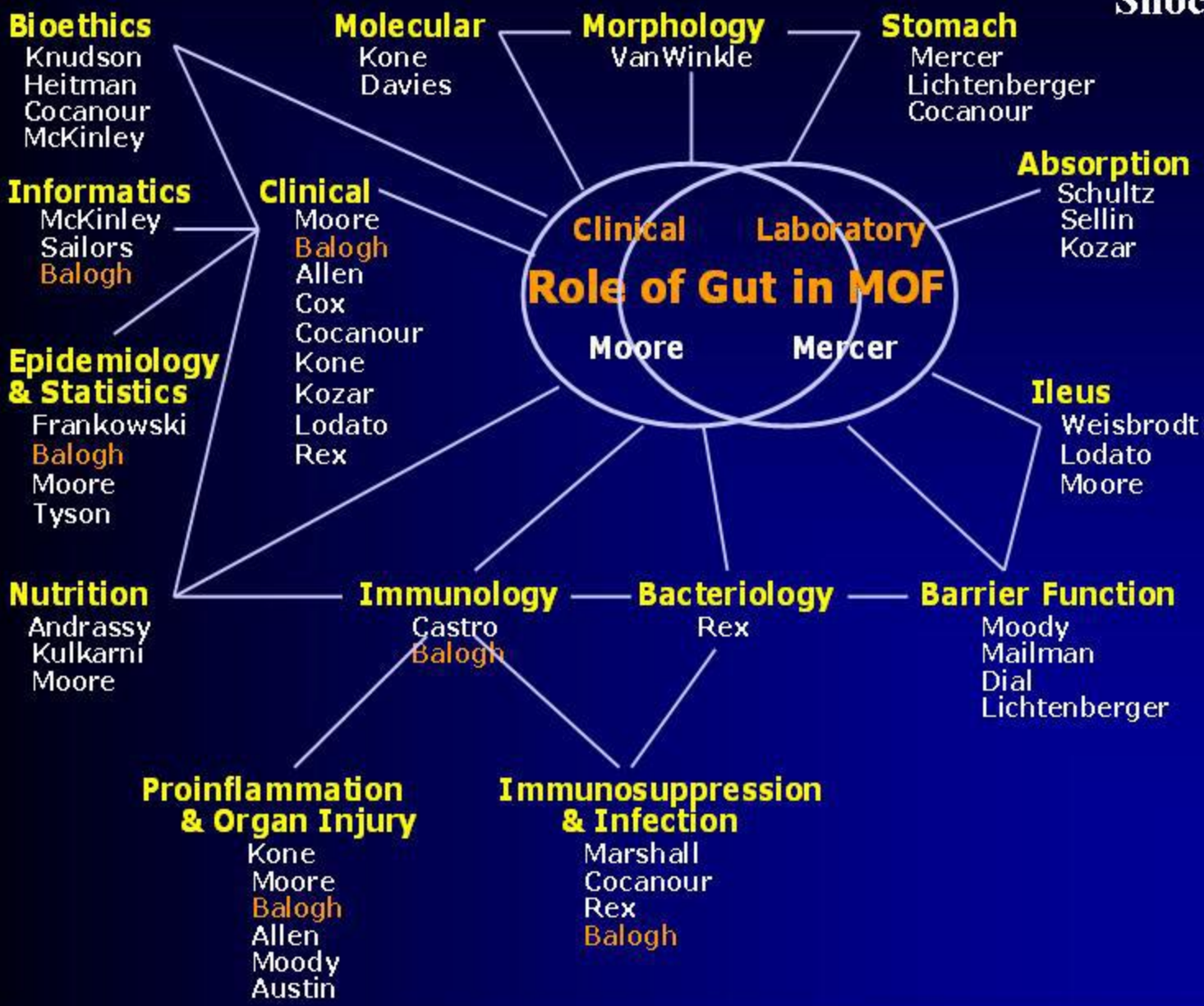
- Identify the risk (Tissue injury, Shock, Age)
- Monitor inflammatory response (IL-6, IL-8)
- Those who met with these:
  - **Neutrophil elastase >85 ng/mL**
  - **Platelet count <180,000 /μL**
  - **CRP >11mg/dL**

  For Planned Interventions


DO2I
700.0
600.0
500.0
400.0
300.0
1
5
9
13
17
21
25
Time (h)
ACS
nonACS

TRAUMA RESEARCH CENTER

Shock 2000



Met inclusion criteria

On ICU admission:
art, PA, NG tonometer catheters
baseline ABG, Hb, lactate

DO_2I goal

Yes

No

Monitor:
lactate, BD, $PrCO_2$
bladder pressure
Q 4h (reassess sooner if abnormal)

1) Hb (PRBC; Hb > 10 g/dL)
2) volume (LR; PAWP ≥ 15 mmHg)

3) Optimize CI - PAWP (Starling curve)

4) low dose inotrope
5) vasopressor

Echo cardiography

24 hours?

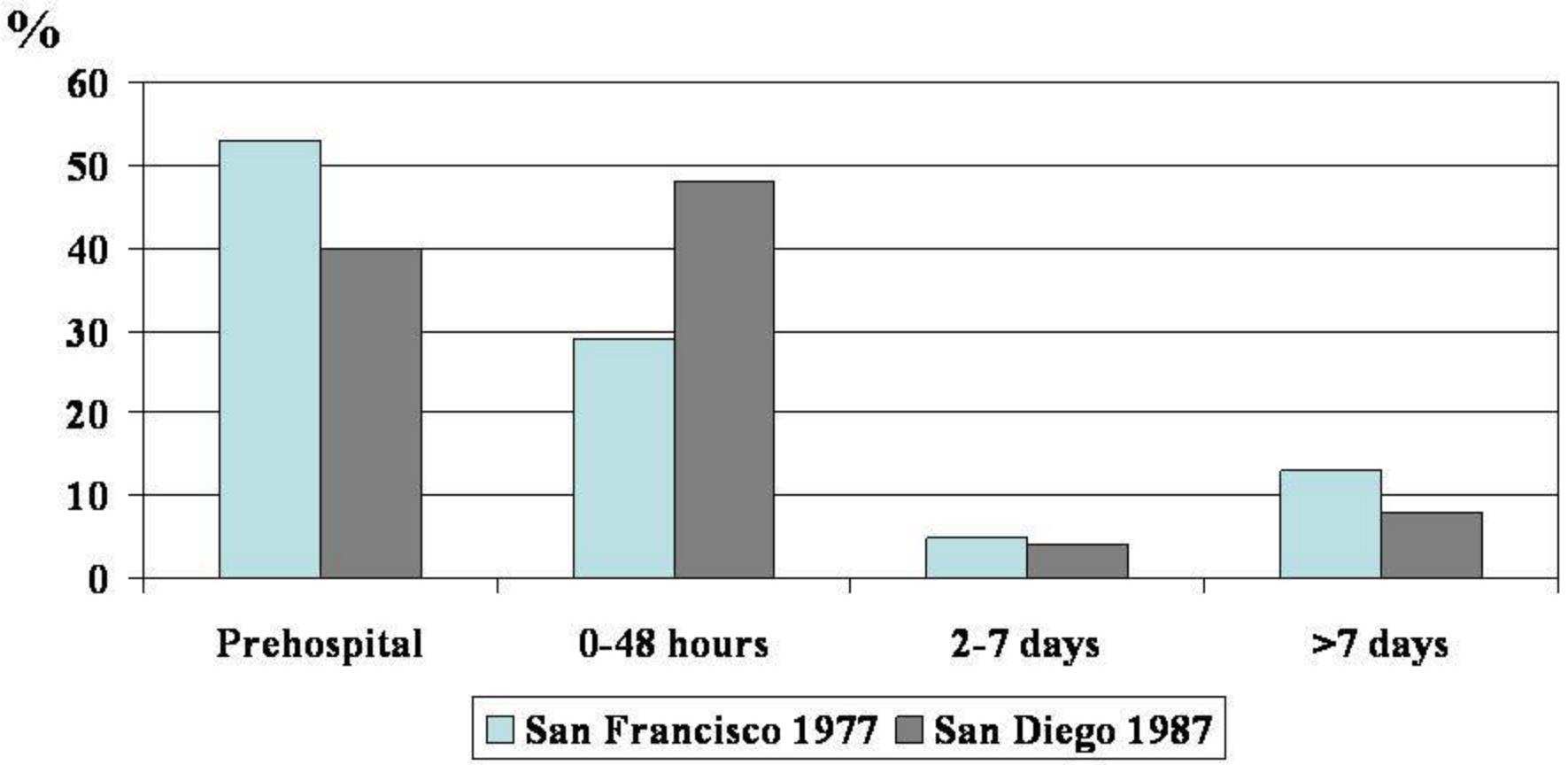
No

Yes

stop resuscitation
standard ICU care

Timeframes (%)

john hunter trauma service



OUTCOME

	1º ACS	2º ACS	Non ACS
MOF (%)	55	53	12[a]
Mortality (%)	64	53	17[a]

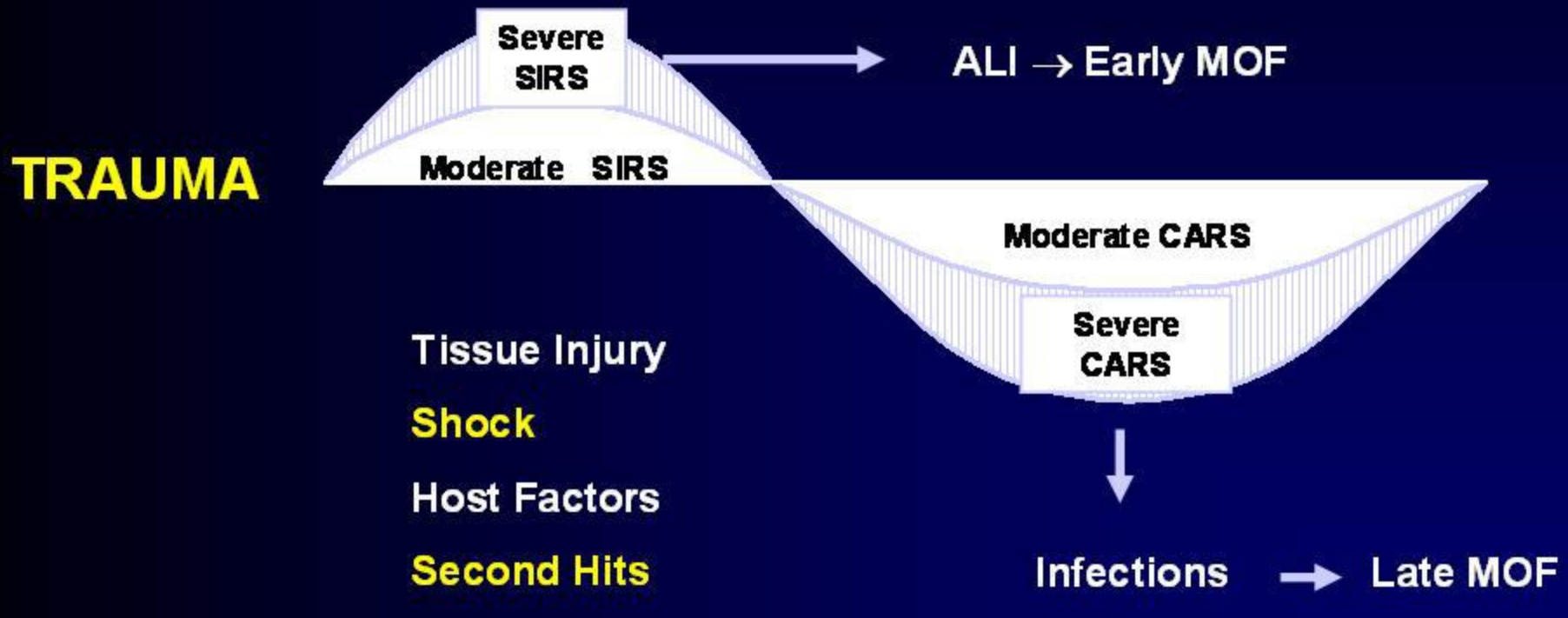
[a] p<0.05 non ACS vs primary or secondary ACS

ACS is an independent risk factor for:

MOF odds ratio = 9.2
95% confidence intervals: 3.8 - 22.8

Mortality odds ratio = 8.4
95% confidence intervals: 3.5 - 20.6

POSTINJURY MOF OCCURS AS A RESULT OF A DYSFUNCTIONAL INFLAMMATORY RESPONSE



TIMING IS EVERYTHING

- The early vulnerable window of PMNs
  - » Botha et al Surgery 1995
- Amplified cytokine response after ACS compared to shock alone
  - » Oda et al. J Trauma 2002
- ACS occurs between 6-8 hours during resuscitation and risk factor for MOF
  - » Balogh et al. J Trauma 2003
- Laboratory data: ACS at 8hrs maximal organ injury
  - » Rezende-Neto et al. J Trauma 2002
  - » Rezende-Neto et al. SHOCK 2003

- Postinjury ACS is a preventable link between traumatic shock and MOF

»*Balogh et al. SHOCK 2003*

Major Advancements

- Early advancements in organ support
- Preventive antibiotics
- Optimisation of Oxygen delivery
- Lung protective ventilation
- Insulin and Cortisol replacement
- Avoiding of supra-normal resuscitation
- Reassessment of Independent Predictors

Can we resuscitate better?

"Supra-normal" versus "Normal" trauma resuscitation

RESULTS

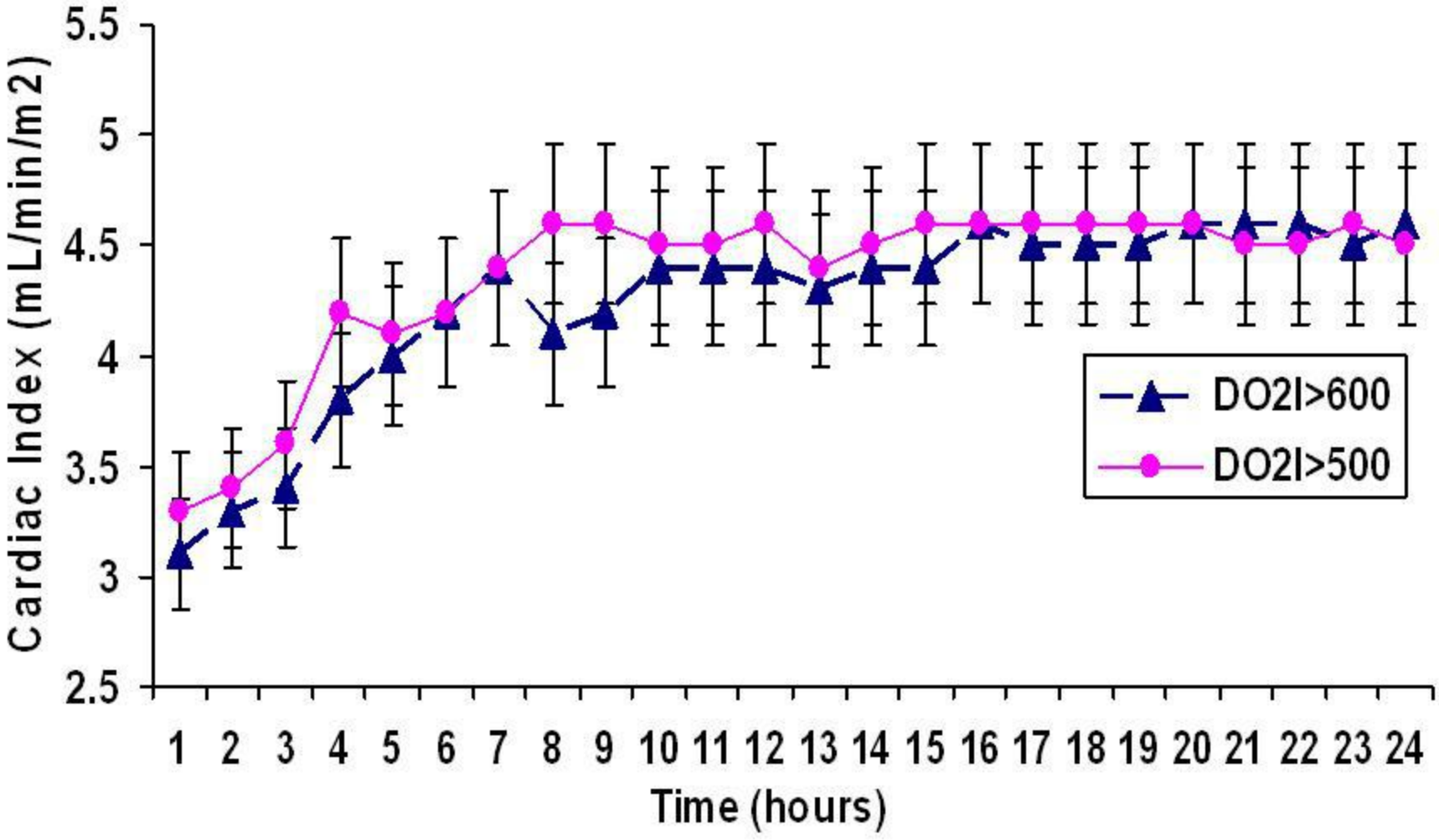
DO_2I_{600} N= 85 DO_2I_{500} N= 71

The groups had similar demographics, ISS and severity of shock.

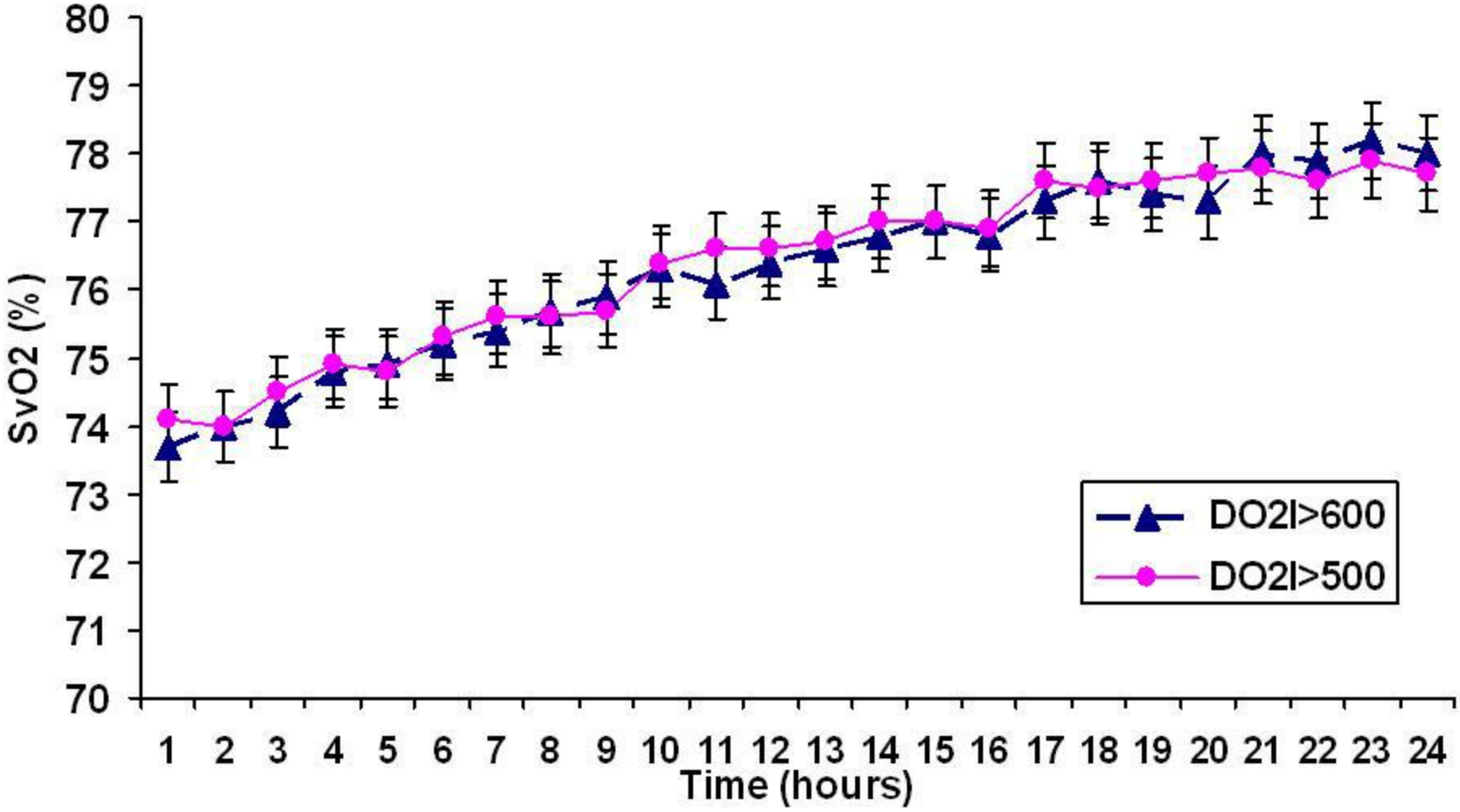
Group	Age (years)	Male (%)	ISS	BD (mEq/L)	Pre-ICU LR (L)	Pre-ICU PRBC (U)
DO_2I_{600}	37 ±3	76	28 ±3	9 ±1	6 ±1	5 ±1
DO_2I_{500}	33 ±2	74	27 ±2	9 ±1	5 ±1	5 ±1

*(mean ±SEM) were analyzed by t and χ^2 tests; * denotes $p<.05$.*

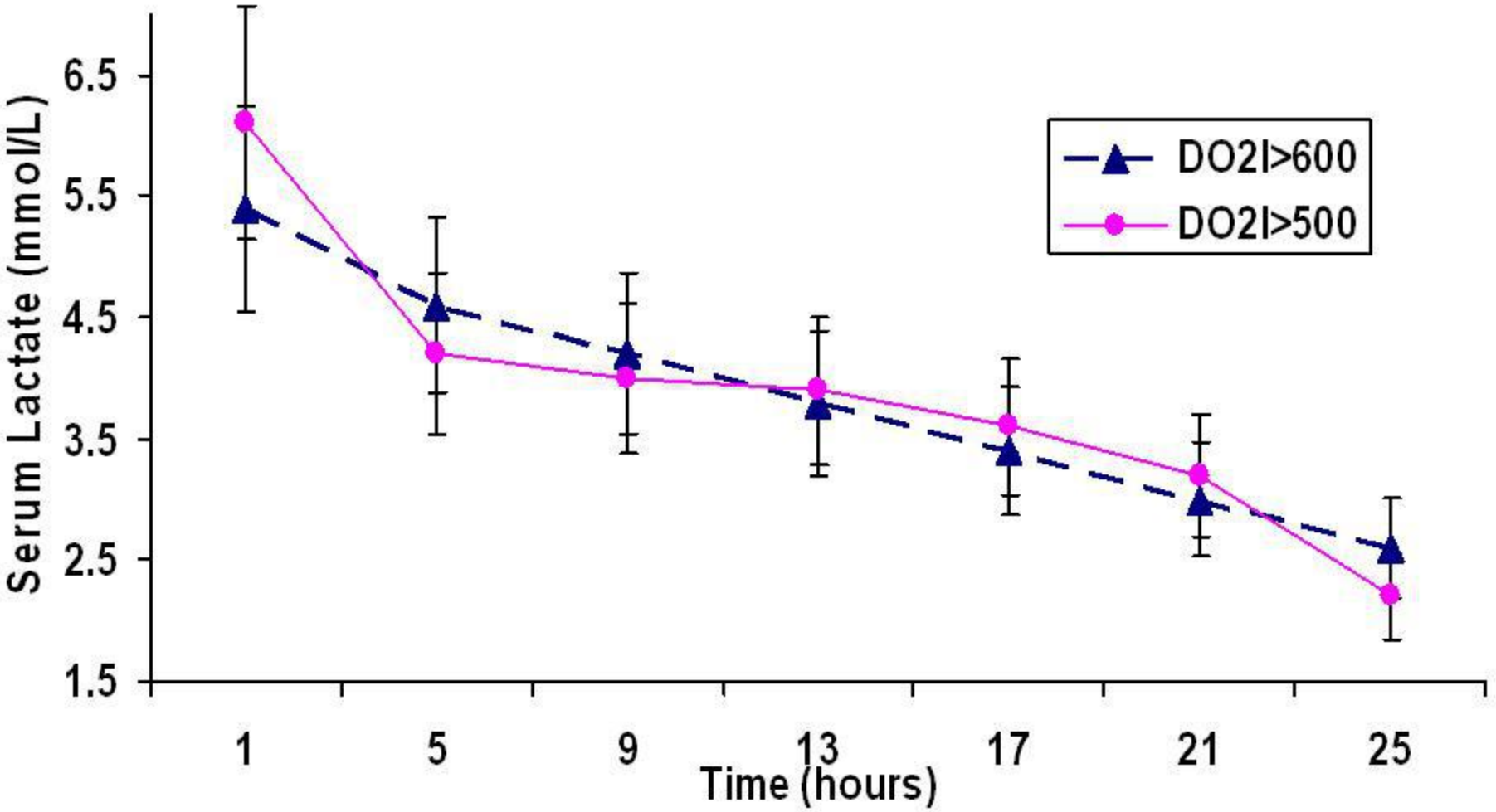
Cardiac Index during ICU resuscitation



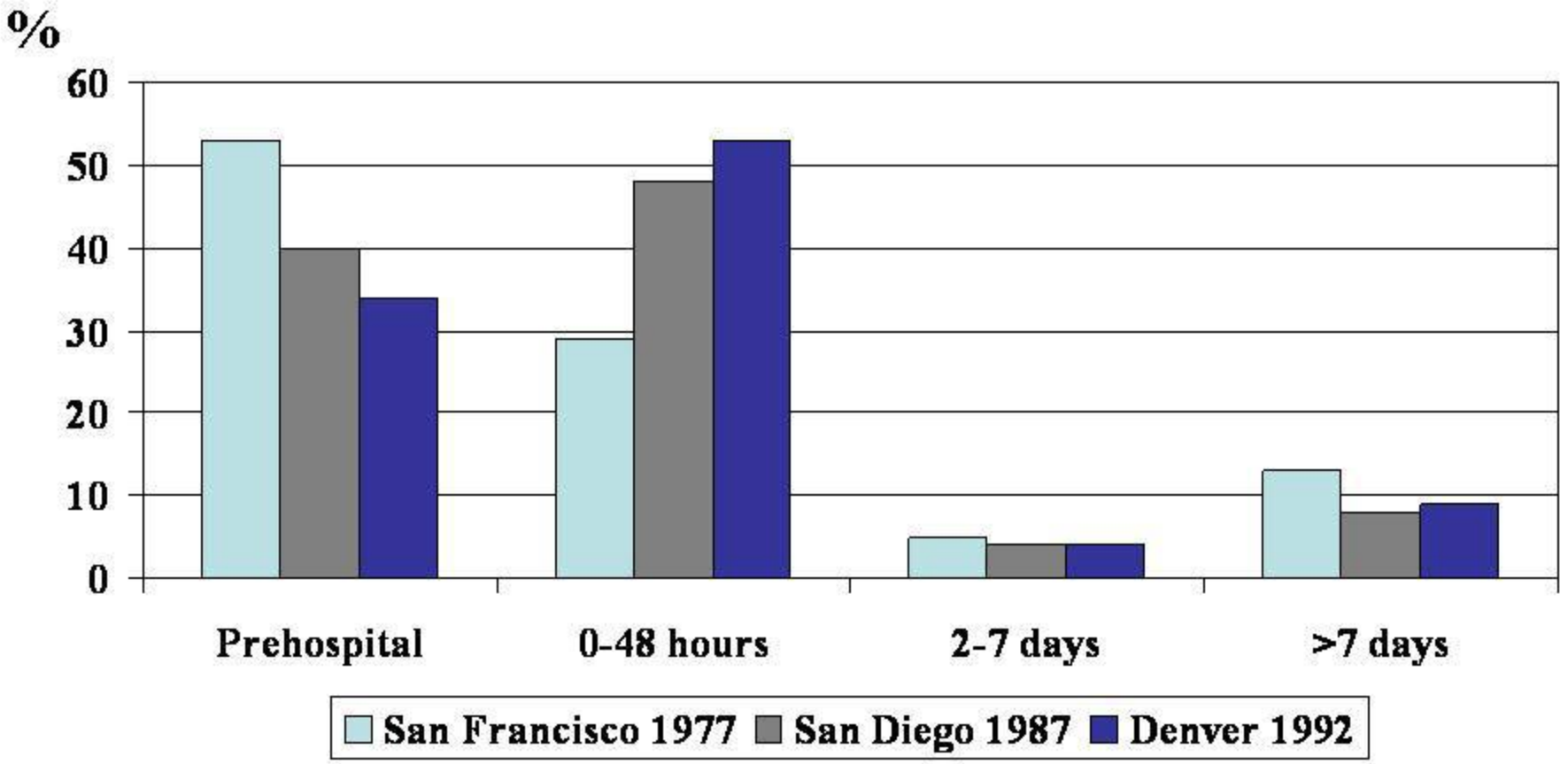
SvO2 During ICU Resuscitation

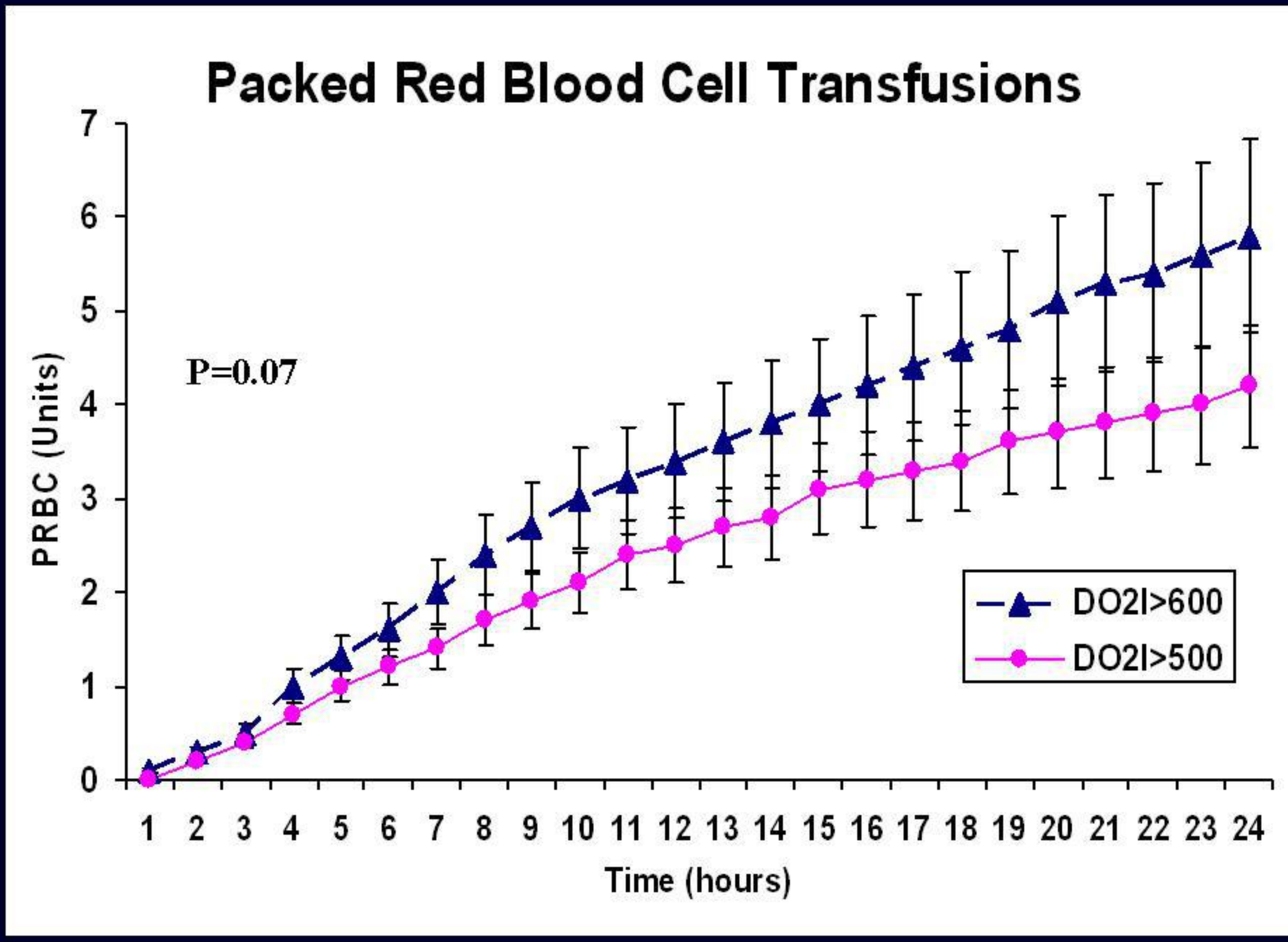


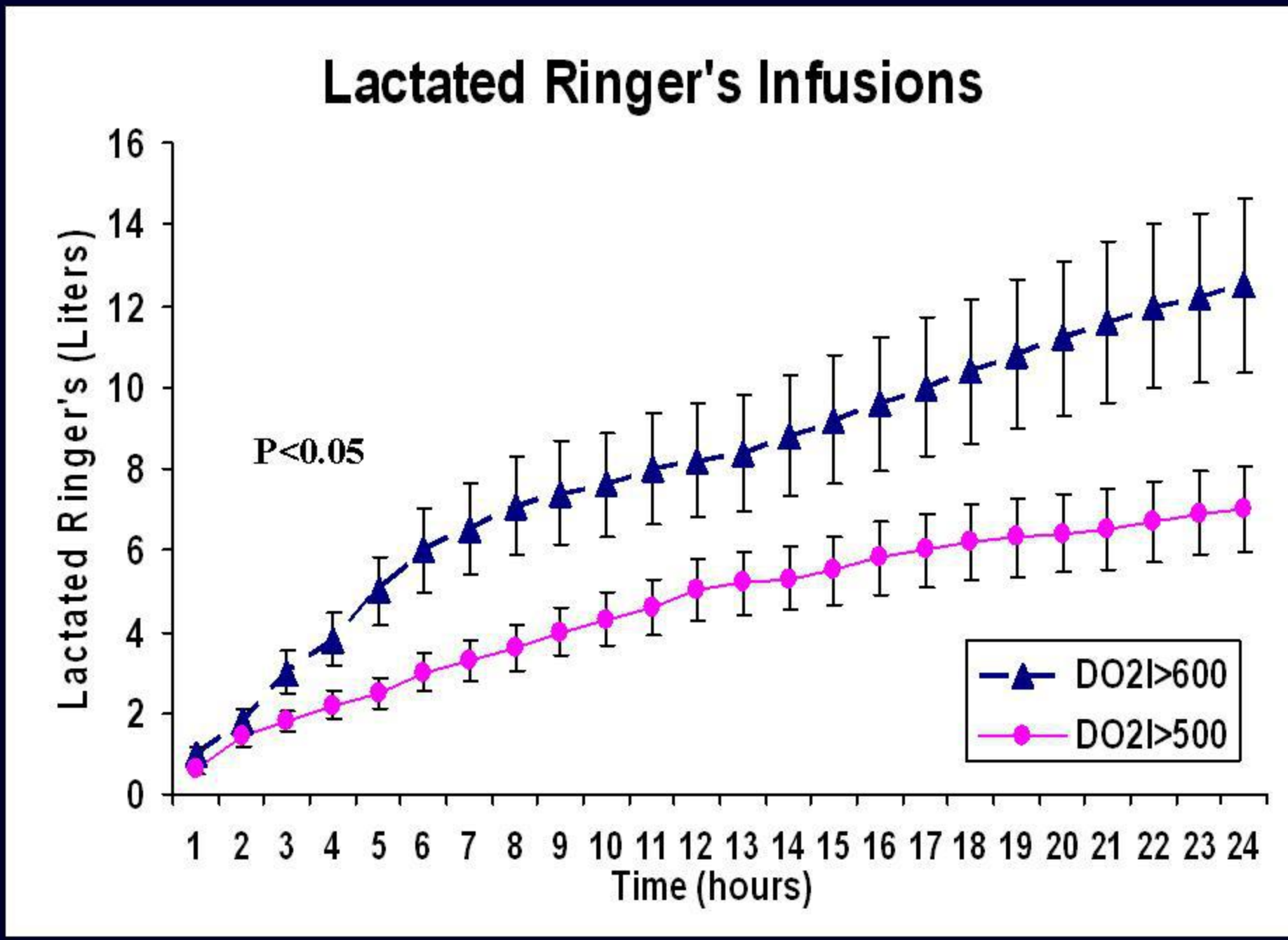
Serum Lactate Concentration

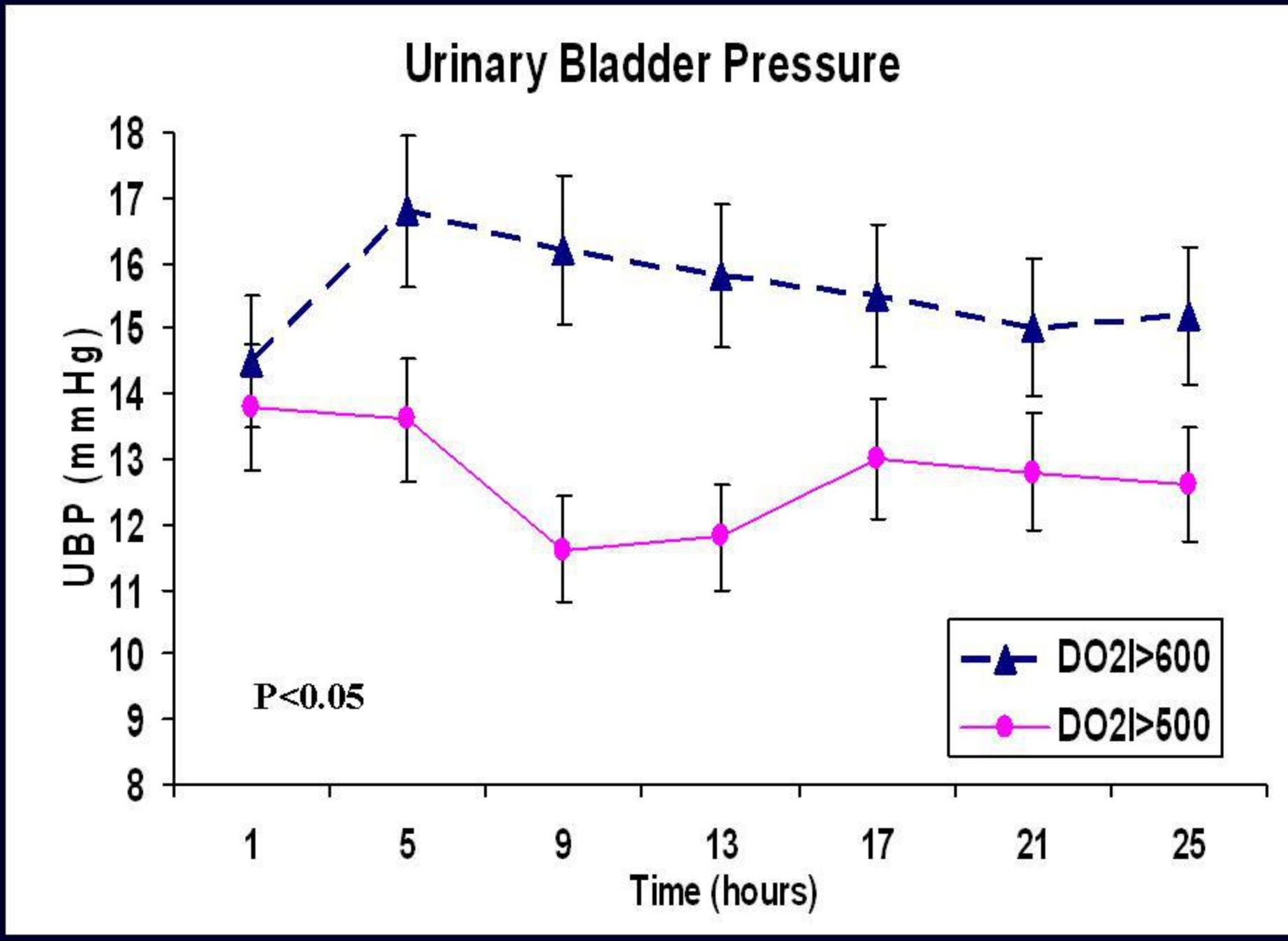


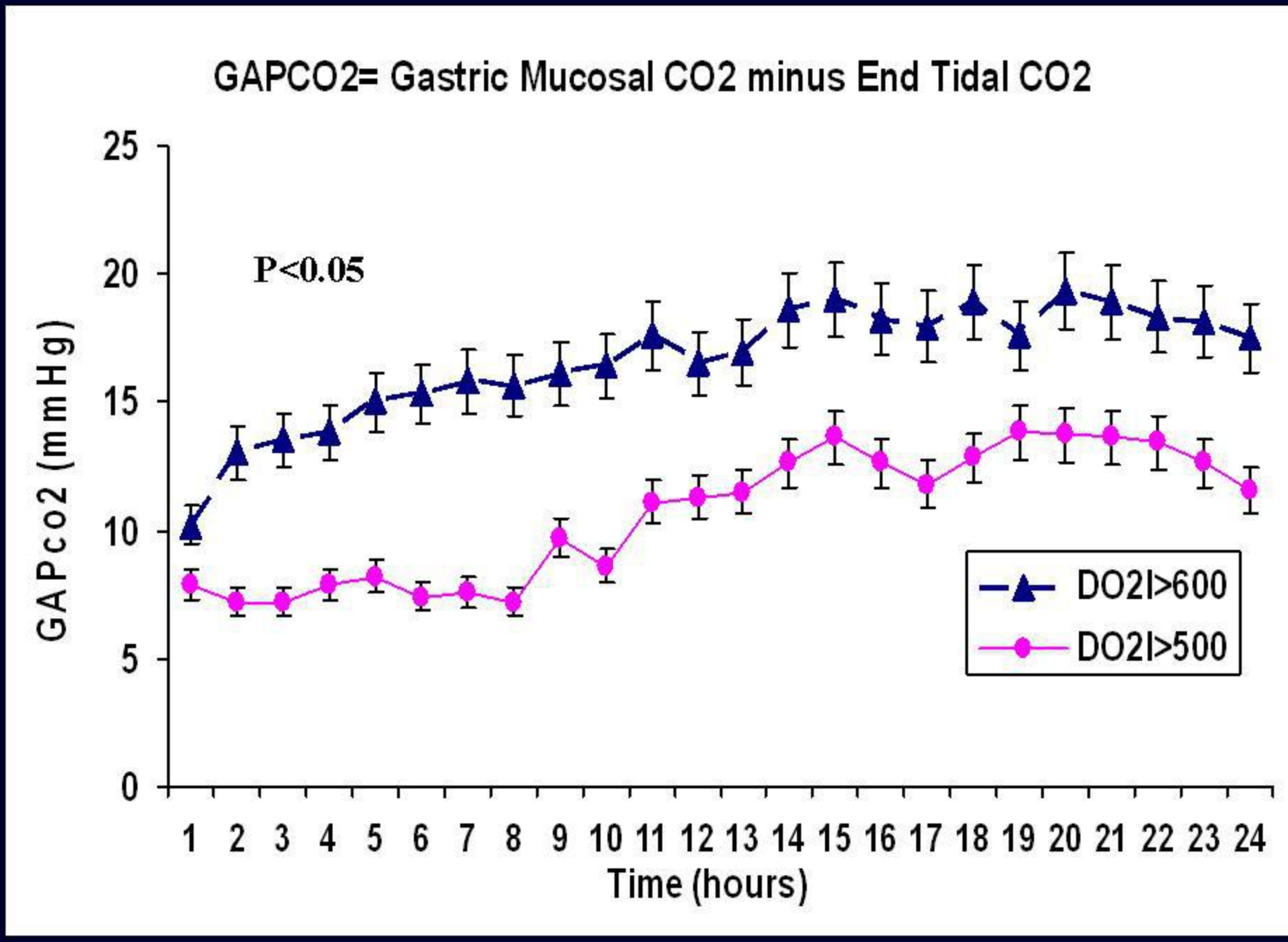
Timeframes (%)


%
60
50
40
30
20
10
0
Prehospital
0-48 hours
2-7 days
>7 days
San Francisco 1977
San Diego 1987
Denver 1992


Packed Red Blood Cell Transfusions
PRBC (Units)
0
1
2
3
4
5
6
7
P=0.07
DO2I>600
DO2I>500
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)


Lactated Ringer's Infusions
Lactated Ringer's (Liters)
0
2
4
6
8
10
12
14
16
P<0.05
DO2I>600
DO2I>500
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)


Urinary Bladder Pressure
UBP (mmHg)
18
17
16
15
14
13
12
11
10
9
8
1
5
9
13
17
21
25
Time (hours)
P<0.05
DO2I>600
DO2I>500


GAPCO2= Gastric Mucosal CO2 minus End Tidal CO2
P<0.05
GAPco2 (mmHg)
25
20
15
10
5
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time (hours)
DO2I>600
DO2I>500

RESULTS

Group	IAH %	ACS %	MOF %	Death %
DO_2I_{600}	42*	16*	22*	27*
DO_2I_{500}	20	8	9	11

*(mean ±SEM) were analyzed by t and χ^2 tests; * denotes $p<.05$.*

Balogh et al. Arch Surg 2003

THE NISS PREDICTS BETTER POSTINJURY MOF THAN THE ISS

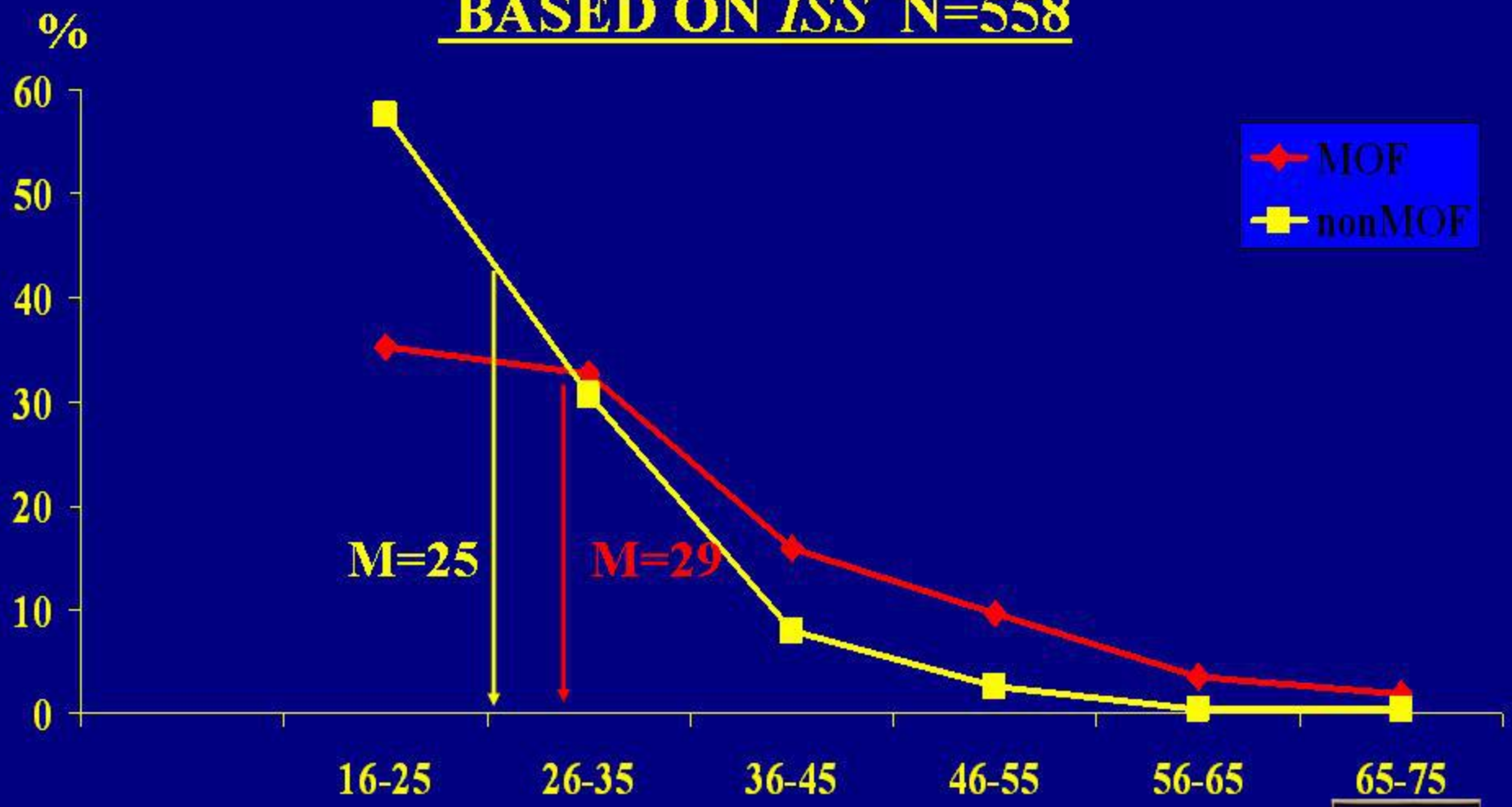
Balogh et al J Trauma 2000

NISS IS BETTER IN MOI THAN ISS

Balogh et al J Orthop Trauma 2003

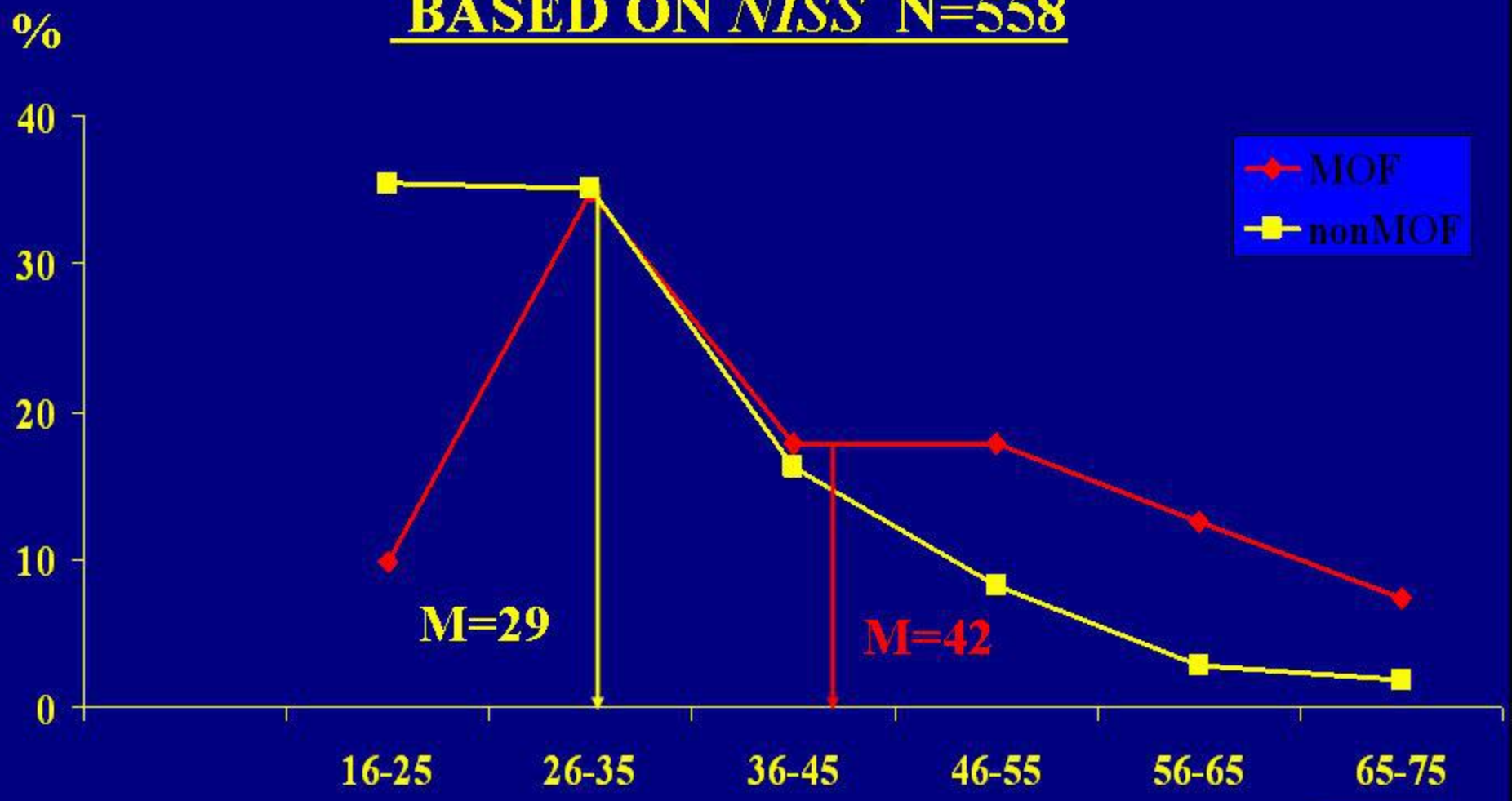
Region	Injury	AIS	ISS	NISS
Head	Concussion	2	2^2	
Face-Neck	Mandible fx	2	2^2	
Chest	Left PTX (minor)	2		
Abdomen	-			
Extremity	C-type pelvic fx	4	4^2	4^2
	Left open femur fx	4		4^2
	Right supracondylar fx	3		3^2
External	Multiple abrasions	1		
			24	**41**

SEPARATION OF MOF AND nonMOF PATIENTS BASED ON *ISS* N=558



The difference of ISS median values: 29 - 25 = 4

SEPARATION OF MOF AND nonMOF PATIENTS BASED ON *NISS* N=558



The difference of NISS median values: 42 - 29 = 13

	Year: 2000	Year: 2006
Age (years)	40	41
Gender (male%)	76%	76%
Mechanism (Blunt%)	85%	97
ISS	29	32
BD (mmol/L)	-9	-7
SBP (mmHg)	93	102
Crystalloid (L/24hrs)	16	12
PRBC (U/24hrs)	9	6
ACS (%)	14	0
MOF (%)	18	9

HISTORY

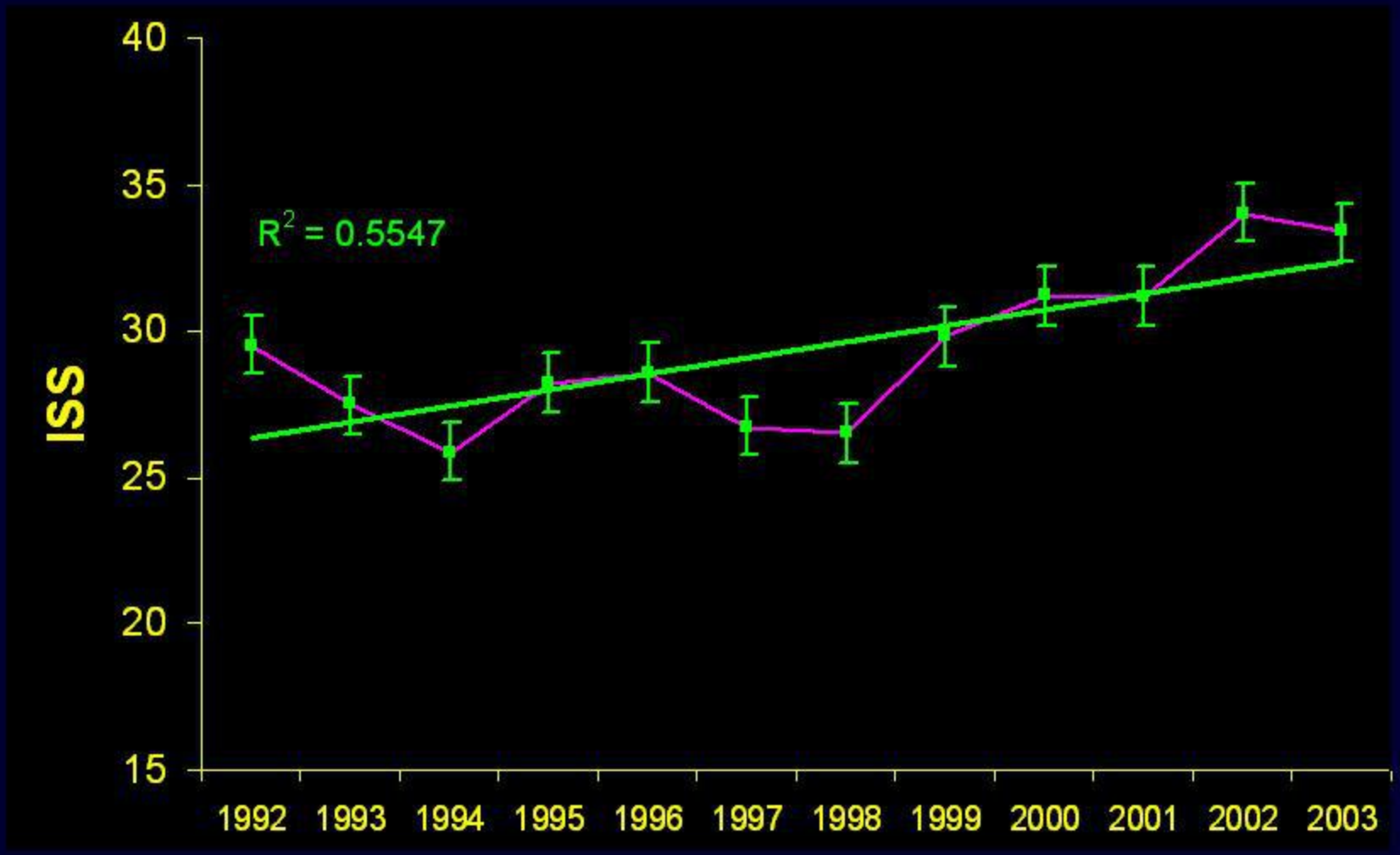
TRAUMA→SHOCK→MOF

Denver MOF Database

- Inclusion Criteria
  - Age > 16
  - ISS > 15
  - Survival > 48h
  - SICU Admit < 48h from Injury
  - No Isolated Head
- Patients
  - 8/18/91 - Present
  - n=1277 as of 9/15/03
  - 72% Male
  - 72% Blunt Mechanism
  - 9% Mortality Rate

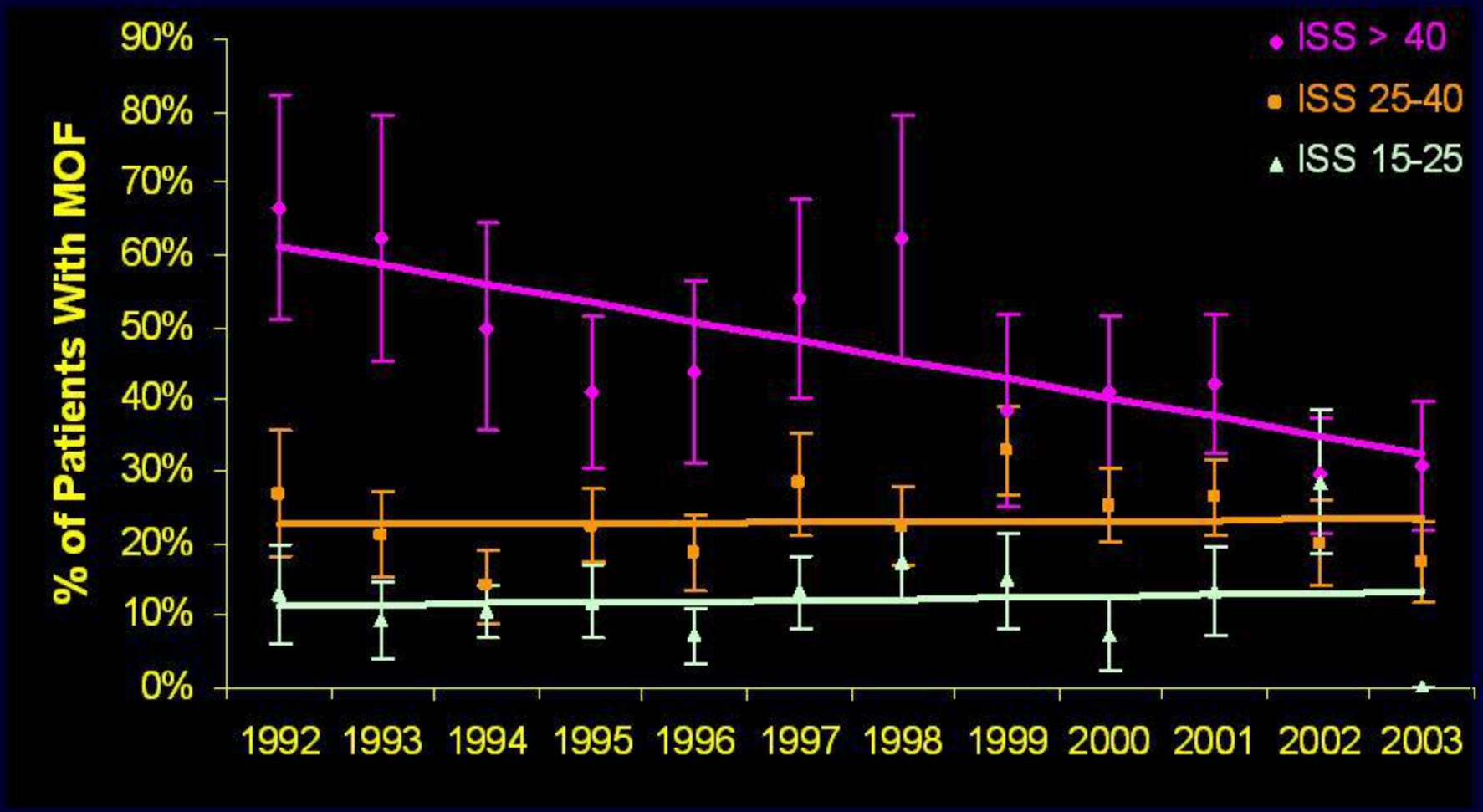
Acknowledgement: DHMC Staff and David Ciesla for the following slides

Injury Severity Over 10 Years

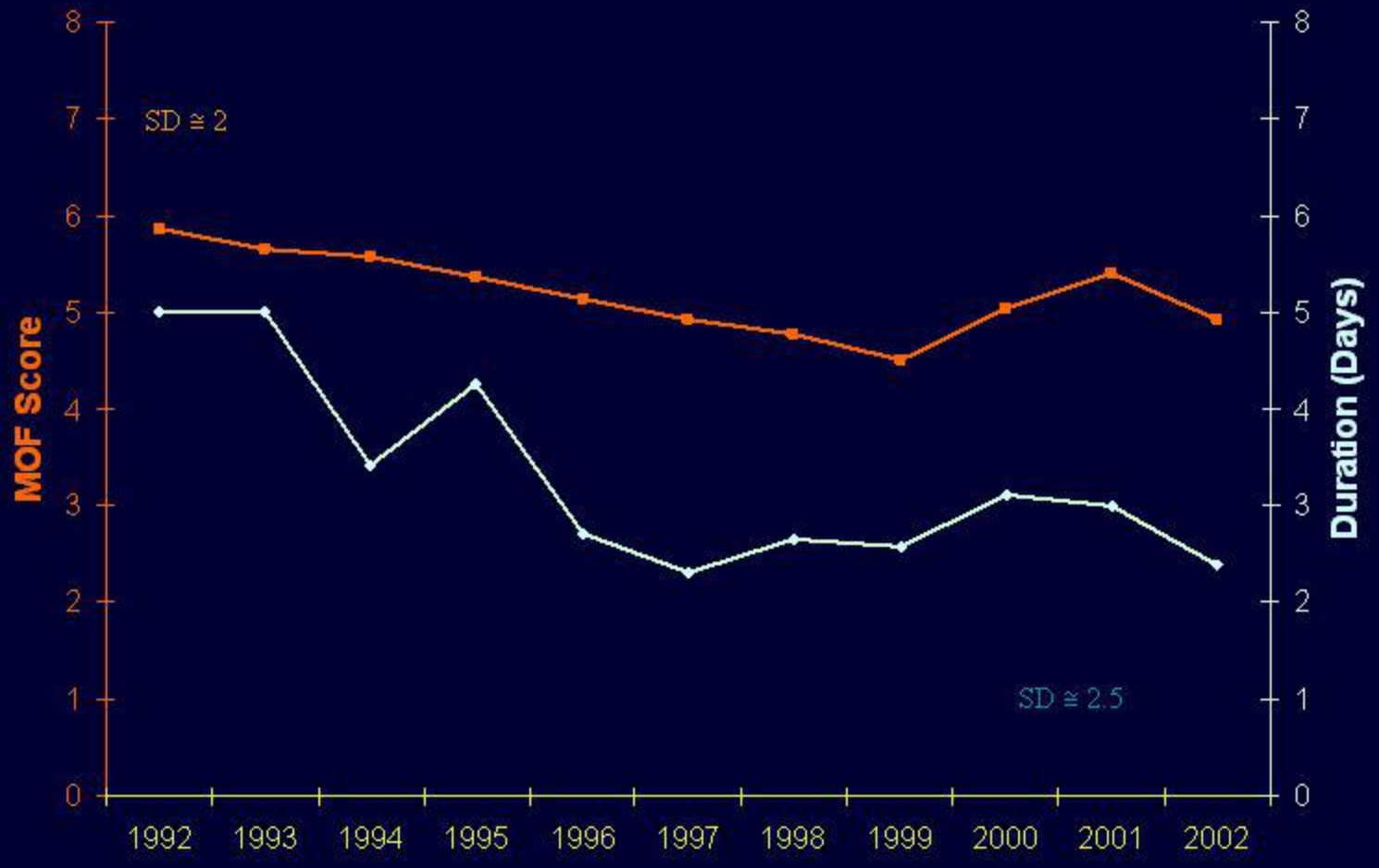


Incidence

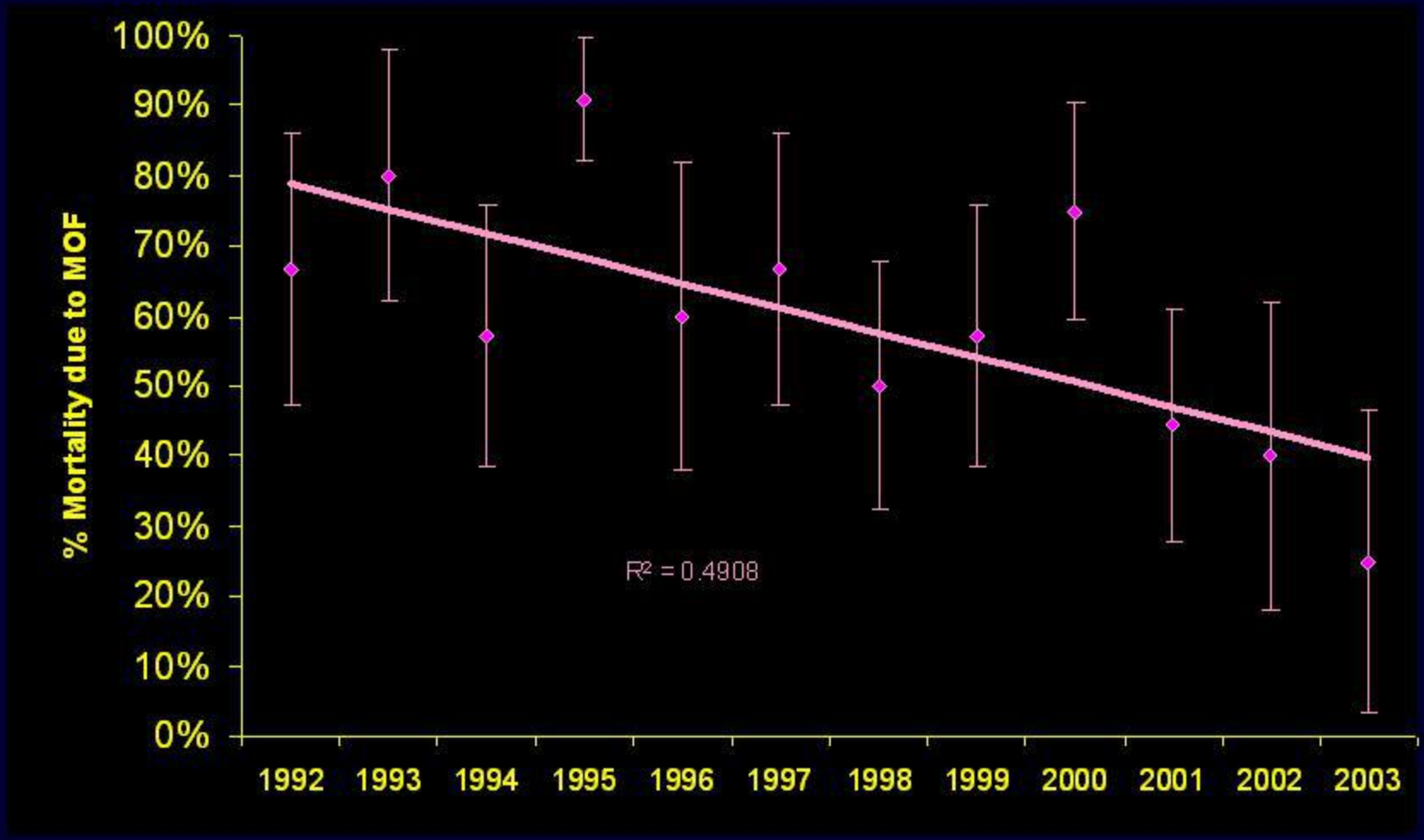
10 Year MOF Rate by ISS



MOF Severity and Duration



Mortality Due to MOF

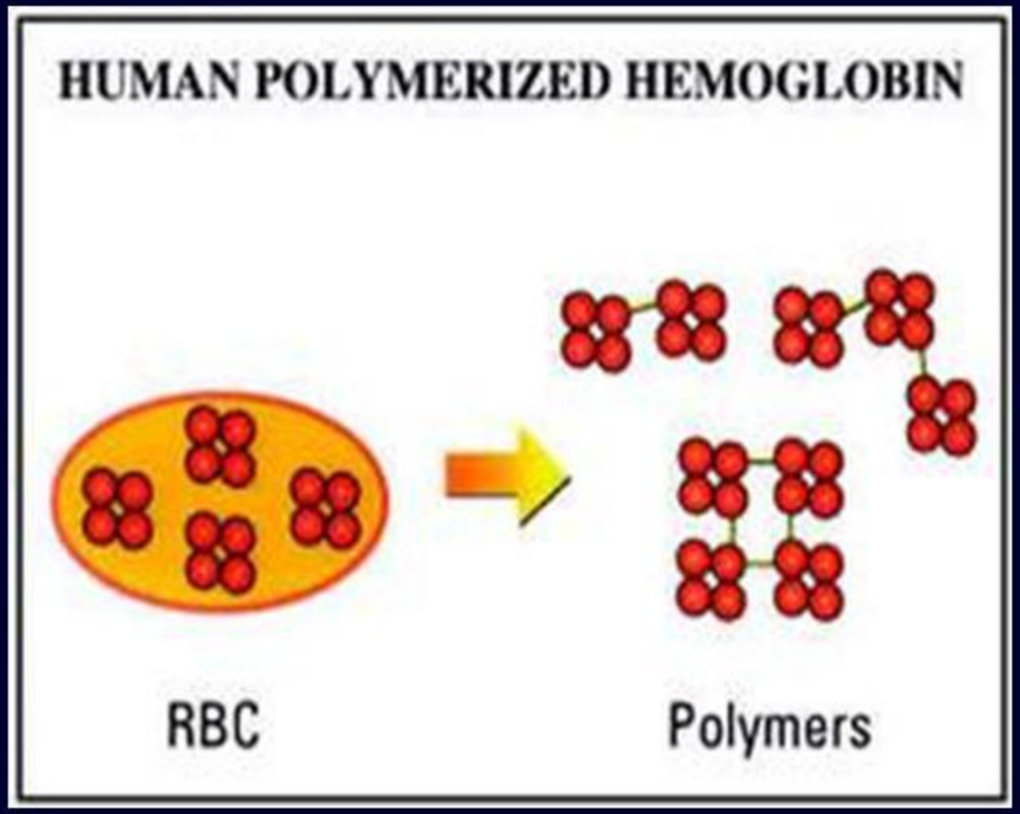


Conclusions

- MOF Rate
  - Postinjury MOF remains a serious clinical problem
  - MOF rates among the most severely injured are decreasing. ISS less predictive.
- MOF Duration and severity
  - People are getting better faster.
- Mortality Rate
  - Mortality rates of patients with MOF is decreasing
  - Mortality due to MOF is decreasing.
- Risk Factors
  - Risk for development of MOF based on earlier models needs to be reassessed given changes in MOF presentation..

Future Directions

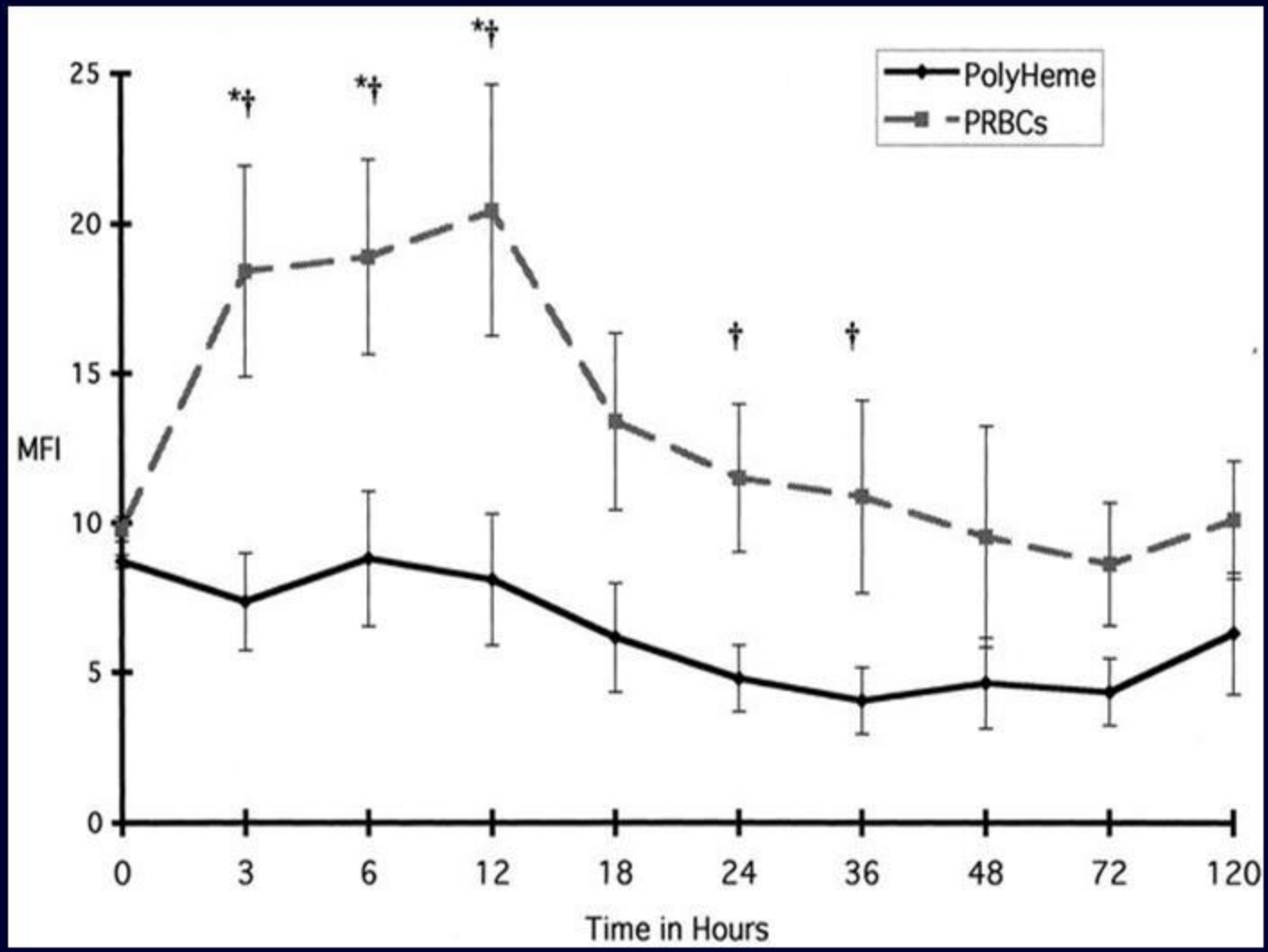
- Reassessment of Independent predictors
- Comparing epidemiology among centres
- Understanding the role of immune-monitoring
- Improvements in fluid resuscitation



- Volume = 500 mL
- Mass Hb = 50 grams
- [Hb] = 10 g/dL
- P_{50} = 28–30 torr
- Met[Hb] < 3%
- Tetramer < 1%
- $T_{1/2}$ = 24 hours
- Shelf life ≥ 1 year

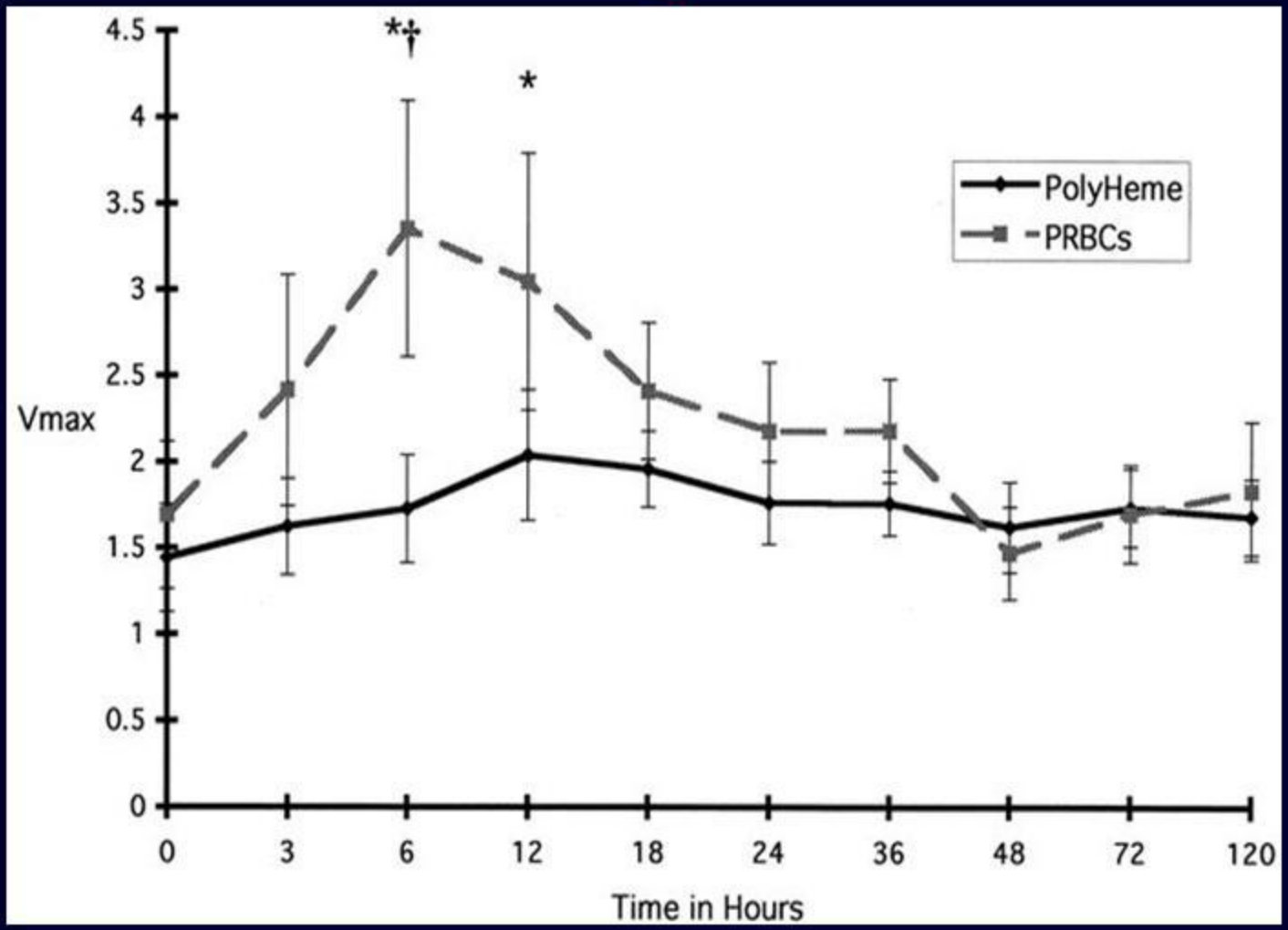
Gould, J Trauma 1997

CD11b



Johnson, J Trauma 2001

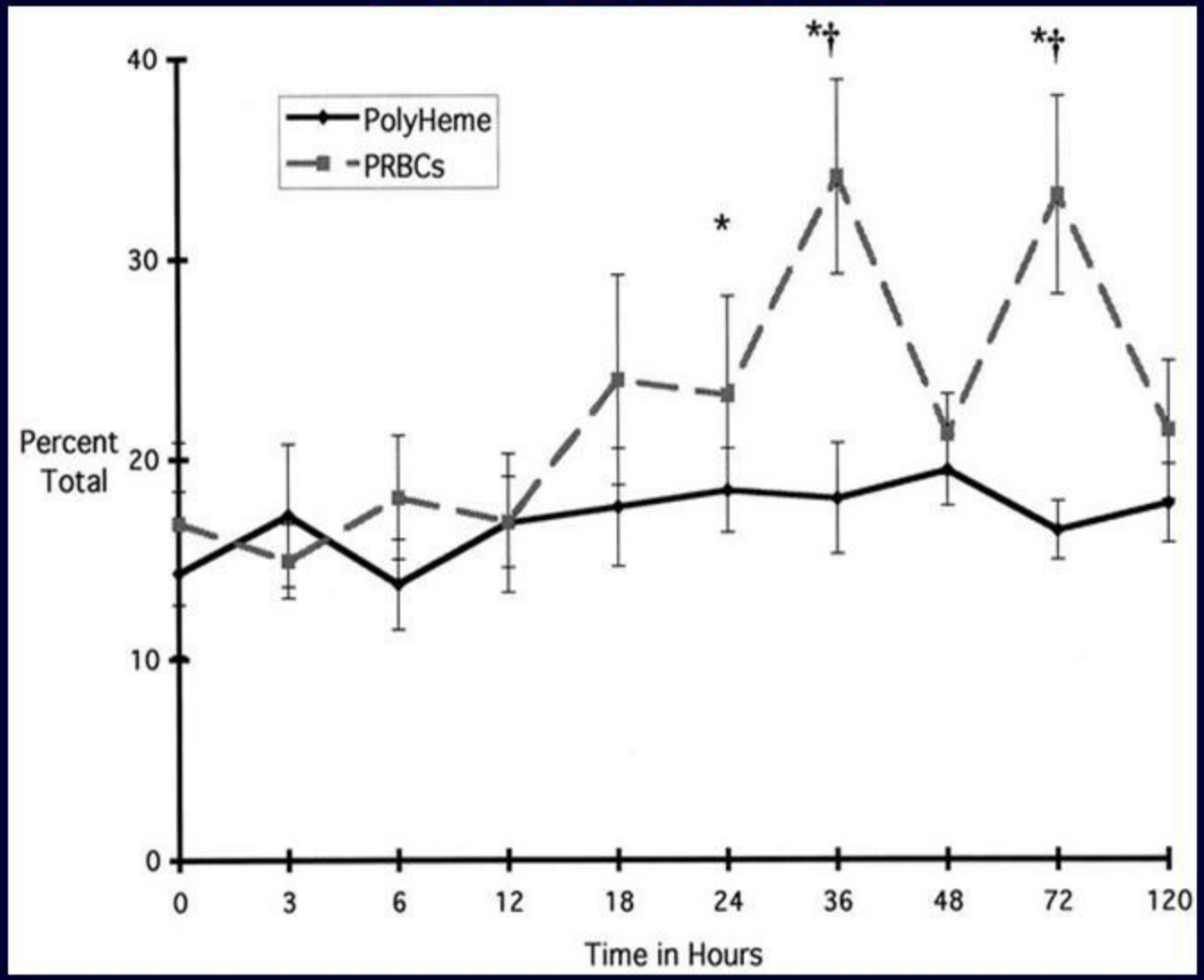
O_2^-



Johnson, J Trauma 2001

TIME	CAUSE	INTERVENTIONS	MANIFESTATION
W.W.I.	Wound toxins	undefined	Cardiac failure
W.W.II.	Blood loss	Normal BP	Renal failure
Korea	Blood loss	Normal BP	Renal failure
Vietnam	Blood loss Extracellular fluid	Urine output Crystalloids	Pulmonary failure
Mid1970 Baue/Eiseman	Shock Age sepsis	Advanced organ support capabilities	Sequential organ failure
Early1980 Polk/Fry	Uncontrolled infection	Prevent and treat septic complications	Infectious models
Late1980 Faist/Goris/Deitch	Systemic inflammation Bacterial transl	Control inciting event, attenuate early inflammation	Inflammatory models
1990 Moore/Shoemaker/ Waydas/Nast-knolb	SIRS/CARS	Supra-normal Resuscitation endpoints, Avoid secondary events	Dysfunctional inflammation
Early2000 ??????????????????	SIRS/CARS Resuscitation related problems	Abandoning supra-normal resuscitation Avoid of resuscitation related complications	Dysfunctional inflammation

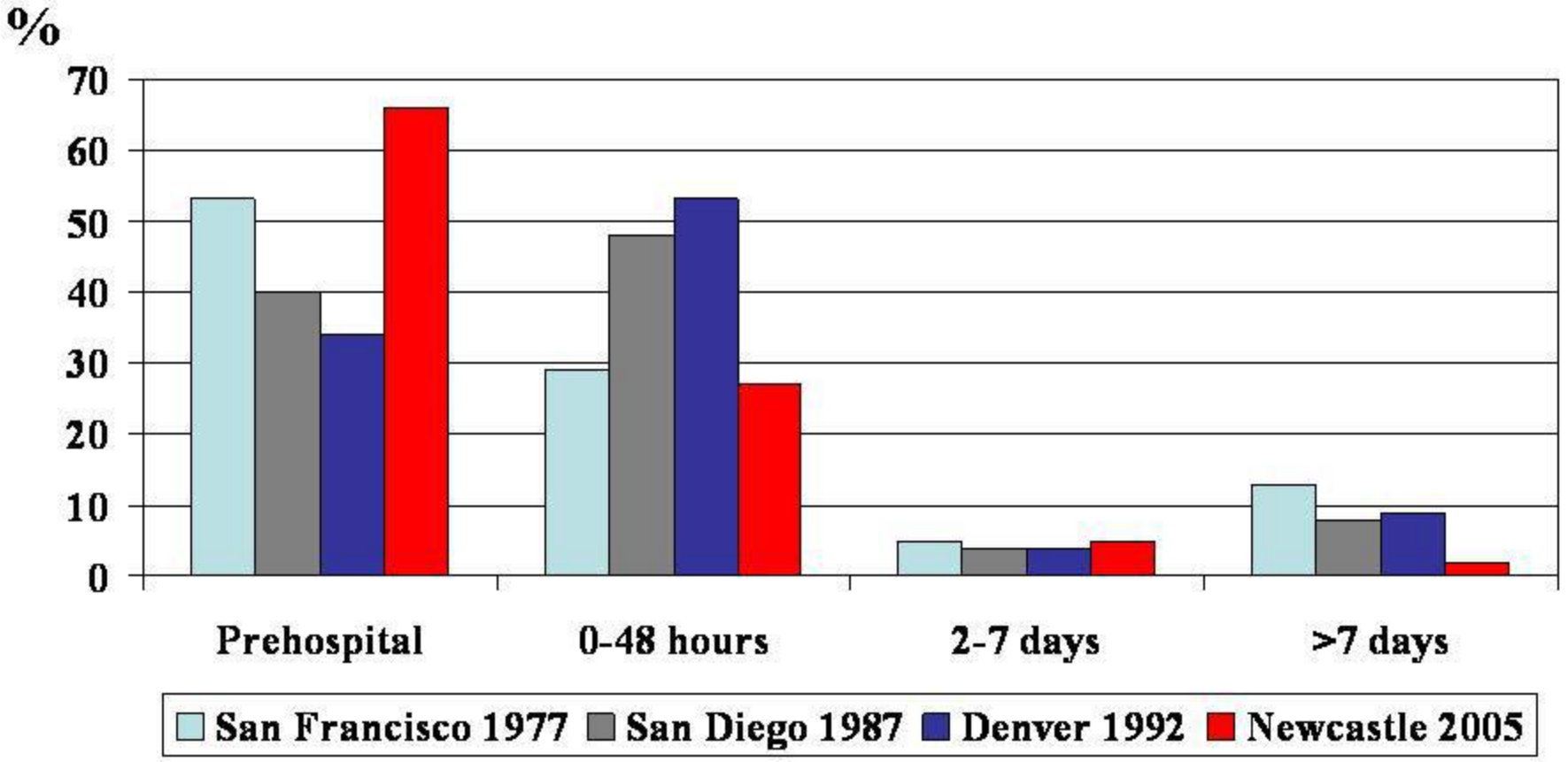
ELASTASE



Johnson, J Trauma 2001

Timeframes (%)

john hunter trauma service



Balogh et al J Trauma in Press

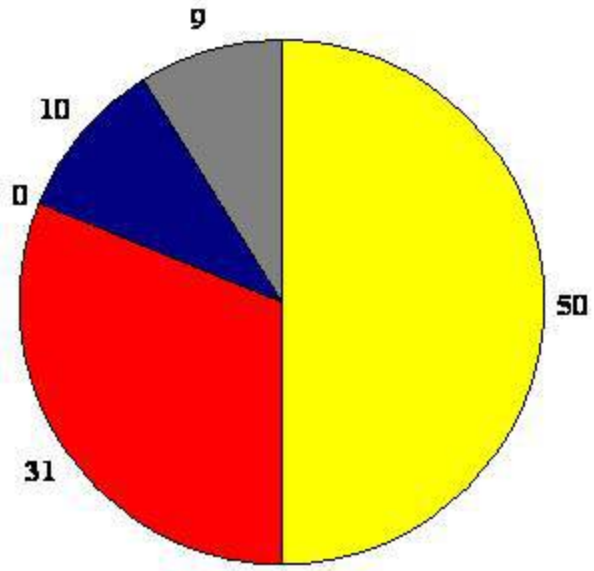
Newcastle Epidemiology

- 2006: 25 patients met inclusion criteria
- 60% male, Age: 39 years, ISS: 27
- 3 patients (12%) had MOF
- Duration: 2.3 days, Severity: 5.7 points
- No Mortality
- 18 vs 7 days on ICU
- The previous predictors are not applicable

Cause of Death (%)

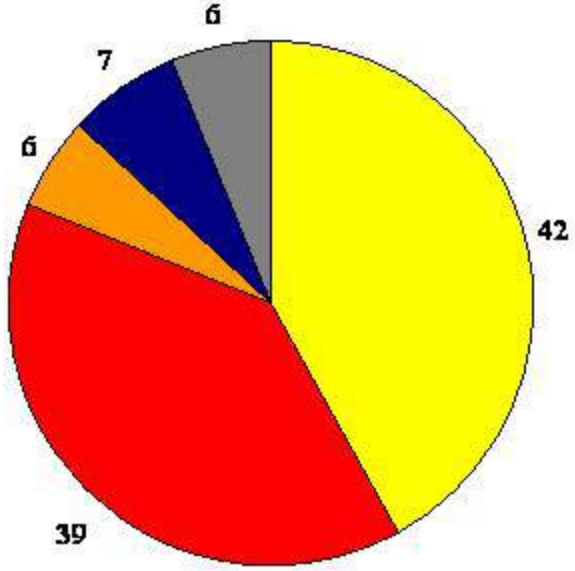
San Francisco 1977

N= 437



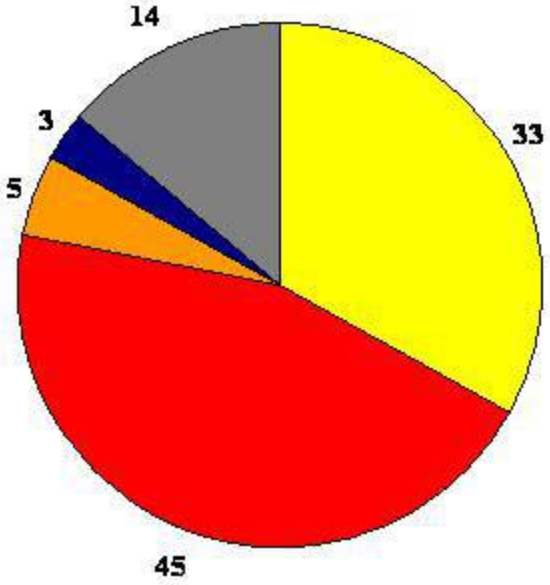
Denver 1992

N= 289



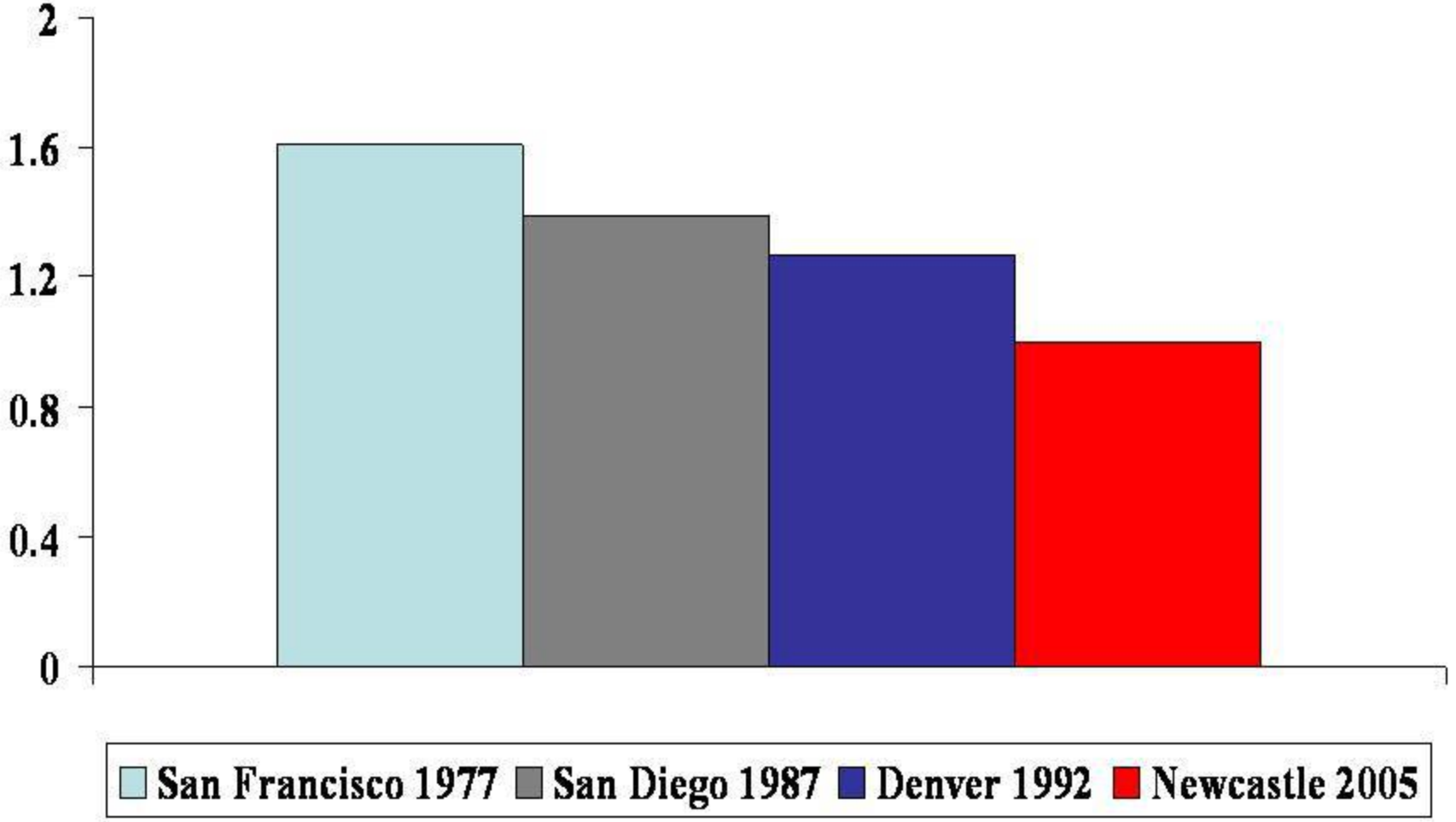
Newcastle 2005

N= 103



CNS | Bleeding | CNS+Bleeding | MOF | Other

Head injury/Exsanguination



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