
**FIRST VIENNA
SHOCK FORUM**
Part B: Monitoring
and Treatment of Shock

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Contents

Contributors	xi
Contents of Part A	xvii
Preface	
Günther Schlag and Heinz Redl	xxi
 1. MONITORING OF SHOCK	
 1.1. Prognostic Indices and Scoring	
Scoring Systems and Predictors of ARDS and MOF	
R. Jan A. Goris, Hans K.S. Nuytinck, and Heinz Redl	3
The Use of Scoring Systems as Prognostic Parameter After Surgery and Trauma	
Peter Lehmkuhl, M. Ludwig, and I. Pichlmayr	17
Prediction of Outcome in Sepsis	
H.B. Stoner	25
Prognostic Indices in Septic Shock	
Jesús Villar, Miguel A. Blazquez, José A. Bolaños, Juan J. Manzano, and José Quintana	33
 1.2. Biochemical Parameters	
Quantification of Granulocyte Enzymes/Proteins With Immunoassays	
H. Lang, S. Neumann, W. Rautenberg, H. Fritz, Marianne Jochum, and D. Inthorn	41
Studies of Granulocyte Function (Chemiluminescence Response) in Postoperative Infection	
Dietrich Inthorn, Thomas Szczeponik, Dieter Mühlbayer, Marianne Jochum, and Heinz Redl	51
Elevated D-erythro-Neopterin Levels in Intensive Care Patients With Septic Complications	
Wolfgang Strohmaier, Heinz Redl, Günther Schlag, and Dietrich Inthorn	59
The Influence of Septic Shock on Plasma Proteins, Lymphocytes and Metabolic Parameters	
Erich Roth, Rudolf Steininger, Ingrid Schindler, Gerhard Hamilton, Walter Mauritz, Friedrich Zekert, Manfred Mattausch, Eva Schönthal, Paul Sporn, and Josef Funovics	67

Inhibition of Beta-FXIIa in Plasma of Volunteers and Polytraumatized Patients	
Günther Fuhrer, Michael J. Gallimore, Wolfgang Heller, and Hans-Eberhard Hoffmeister	77
Can the Outcome After Trauma or Sepsis be Predicted From Biochemical or Hormonal Parameters?	
Thomas Pasch, Jörg Mahlstedt, Josef Pichl, Gernot Buheitel, and Edgar Pscheidl	85
The Proenzyme Functional Inhibition Index as a Predictor in Septicemia	
Ansgar O. Aasen	97
1.3. Hemodynamic Parameters	
Physiologic Monitoring and Therapy of High Risk Surgical Patients	
William C. Shoemaker	103
Hämodynamic Pattern in Septic Peritonitis	
Heinz Köhler, W. Reichow, J. Martell, G. Köveker, and A. Schafmayer	109
Early Metabolic and Vascular Tone Patterns in Lethal Sepsis	
Ivo Giovannini, Giuseppe Boldrini, Carlo Chiarla, Marco Castagneto, and Giancarlo Castiglioni	115
Judgement of Central Haemodynamics With and Without Swan Ganz Catheter in Septic Shock States	
Gerhard Redl, Ernst Zadrobilek, Ingrid Schindler, Walter Mauritz, and Paul Sporn	123
Hemodynamic Characterization of Sepsis	
K. Lenz, A. Laggner, W. Druml, G. Graninger, G. Grimm, and B. Schneeweiß	129
1.4. Extravascular Lung Water	
Intravascular Starling Forces and Extravascular Lung Water in Advanced Septic Shock States	
Ernst Zadrobilek, Ingrid Schindler, Gerhard Redl, Walter Mauritz, Hermann Gilly, Paul Sporn, and Karl Steinbereithner	139
Dynamics of Extravascular Lung Water in Major Burns	
Anton N. Laggner, Kurt Lenz, Gernot Sommer, Wilfred Druml, Bruno Schneeweisz, Georg Grimm, and Gunter Kleinberger	145
Extravascular Lung Water and Pulmonary Artery Pressure With Acute Respiratory Failure—Effect of Ketanserin Administration	
W. Heinrichs, U. Fauth, and M. Halmágyi	153
2. TREATMENT OF SHOCK	
2.1. Basic Supportive Therapy	
Prevention of ARDS and MOF by Prophylactic Mechanical Ventilation and Early Fracture Stabilisation	
R.J.A. Goris	163

Modern Strategies of Ventilatory Management in Shock	
H. Benzer, M. Baum, J. Koller, W. Koller, G. Kroesen, and N. Mutz	175
Therapeutic Approaches: Haemodynamic and Respiratory Complications in Septic Shock	
P. Lawin, H.J. Lübbesmeyer, M. Möllmann, N. Mertes, and H. Van Aken	185
2.2. Volume Replacement	
Fluid Resuscitation in Canine Traumatic-Hemorrhagic Shock: Long-Term Comparison of Hydroxyethyl Starch vs. Ringer's Lactate	
Uwe B. Brückner, Michael Albrecht, Lorenz Frey, and Lars-G. Hein	197
Treatment of Experimental Mesenteric Shock by Different Fluids	
János Hamar, Joachim Lutz, László Dézsi, and Miklós Juhász	205
Does Isovolemic Hemodilution Predispose to Infection?	
Wolfgang Graninger, Franz X. Lackner, Reswan Khosropour, Christine Hlozaneck, and Robert Kurz	209
2.3. Plasmapheresis and Hemofiltration	
Plasma Exchange in Septic Shock	
Lars J. Bjertnaes	215
Continuous Pump Driven Hemofiltration (CPDHF) in Septic Renal Failure	
Paul Sporn, Walter Mauritz, Gerhard Redl, Ingrid Schindler, Karl Steinbereithner, and Ernst Zadrobilek	225
Continuous Arterio-Venous Hemofiltration for the Treatment of Acute Renal Failure in Septic Shock	
Wolfgang Reichow, Heinz Koehler, Klaus Dietrich, and Anton Schafmayer	235
The Continuous Arterio-Venous Hemofiltration in Shock	
H.C. Rau, K.H. Staubach, C. Hohlbach, and W. Klingler	241
2.4. Corticosteroids	
Corticosteroids in the Treatment of Septic Shock	
William Schumer	249
Effect of Methylprednisolone, Prednisolone and Dexamethasone on Granulocyte Function and Complement Activation	
Heinz Redl, Herbert Lamche, Eva Paul, Anna Schiesser, and Günther Schlag	261
Comparison of Different Corticosteroids in Rat Endotoxemia	
Soheyl Bahrami, Anna Schiesser, Heinz Redl, and Günther Schlag	273
Can Preoperative High Dose Corticosteroids Preserve Normal Pulmonary Permeability and Homeostasis?	
Lennart Smith, Svenerik Andreasson, Tom Saldeen, and Bo Risberg	287
2.5 Specific Measures	
Influence of Parenteral Nutrition on Lung Surfactant in the Traumatized Rat	
Soheyl Bahrami, Harald Gasser, Wolfgang Strohmaier, Heinz Redl, and Günther Schlag	295

Effects of Surfactant Replacement on Respiratory Failure Induced by Free Oxygen Radicals	
B. Lachmann, O.D. Saugstad, and W. Erdmann	305
Glucose-Insulin-Potassium (GIK) in Hypodynamic Septic Shock	
Walter Mauritz, Ingrid Schindler, Ernst Zadrobilek, and Paul Sporn	315
Non-Adrenergic Inotropic Support in Septic Shock	
Marc Domb, Corinne De Boelpaepe, and Jean-Louis Vincent	319
Effects of Endotoxin and Gadolinium Chloride on Acute Septic Peritonitis and Septic Shock in Rats	
George Lázár, Jr., Elizabeth Husztik, and George Lázár	323
Index	329

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Contents of Part A: Pathophysiological Role of Mediators and Mediator Inhibitors in Shock

1. THE PATHOPHYSIOLOGICAL ROLE OF MEDIATORS AND INHIBITORS THEREOF IN SHOCK

1.1. Complement—Granulocytes

Complement Activity in Shock / Mats Heideman and Anders Bengtson

Inflammatory Mediators in Patients With Ischemic Limbs / Anders Bengtson, Pia Holmberg, and Mats Heideman

Granulocytes as Mediators of Tissue Injury in Shock: Therapeutic Implications / Dale E. Hammerschmidt and Gregory M. Vercellotti

Role of Fibrin-Neutrophil Interactions in Lung Vascular Injury / Asrar B. Malik

Quantitative Estimation of Leukostasis in the Posttraumatic Lung—Canine and Human Autopsy Data / Heinz Redl, Hans P. Dinges, and Günther Schlag

Whole Body Inflammation in Trauma Patients; an Autopsy Study / Hans K.S. Nuytinck, Xavier J.M.W. Offermans, Karel Kubat, and R. Jan A. Goris

White Cells in Shock Ischemia / David H. Lewis, Anders Gidlöf, Kristina E-dr. Behm, Maj-Britt Bengtsson, and Angela Menschik

Neutrophil Protease Enzymes and Oxygen Free Radicals as Mediators of Pulmonary Membrane Damage / Stephen Westaby

1.2. Proteases

Studies on Shock During Extracorporeal Circulation During Aorto-Coronary Bypass Operations / Wolfgang Heller, Günther Fuhrer, Hans-Eberhard Hoffmeister, and Michael J. Gallimore

Biochemical Monitoring of the Lung During and After Extracorporeal Circulation / Geza Horpacsy, Werner Hügel, Hugo Müller, and Alfred Geißler

Effect of Elevated C1-Esterase Inhibitor Levels on Elastase Release In Vitro—A Proposed Model of Shock (ECC) / Wolfgang Heller, Günther Fuhrer, Susanne Hoberg, Hans-Eberhard Hoffmeister, and Anton Philapitsch

Granulocyte Elastase and White Cell Counts in Septic Pigs / M. Siebeck, H. Hoffmann, and R. Geiger

Influence of the Lysosomal Elastase Inhibitor Eglin on the Development of Interstitial Lung Edema in *E. coli* Bacteremia in Pigs / H.F. Welter, M. Siebeck, O. Thetter, and M. Jochum

Evaluation of the Kinin-Induced Pathomechanisms in the Development of ARDS by Kallikrein Inhibition In Vivo / O. Thetter, H. Hoffmann, M. Siebeck, H.F. Welter, and H. Fritz

Local Activation of the Kallikrein-Kinin System in the Lung Following *E. coli* Sepsis in Sheep / Svenerik Andreasson, Lennart Smith, Ansgar O. Aasen, and Bo Risberg

C1-Esterase Inhibitor in Early Septicemia / M. Siebeck, A. Philapitsch, H. Wiesinger, and H.F. Welter

Anti-Proteases in Endotoxemia / Daniel L. Traber

Effect of Aprotinin and C1-Esterase Inhibitor on Activation of the Plasma Kallikrein-Kinin System In Vivo / H. Hoffmann, M. Siebeck, O. Thetter, E. Fink, and A. Philapitsch

xviii / Contents of Part A

Cellular Effects of Aprotinin / Heinz Redl, Anna Schiesser, Eva Paul, Claudia Wilfing, and Günther Schlag

Feasibility Study of Very High Aprotinin Dosage in Polytrauma Patients / C. Clasen, M. Jochum, and W. Mueller-Esterl

Hemodynamics and Proteolysis in Experimental Trypsin Induced Shock / Froye Naess, Johan Pillgram-Larsen, Tom E. Ruud, Jan O. Stadaas, and Ansgar O. Aasen

Protease Inhibitor Infusion Improves Survival Rate and Hemodynamics in Experimental Pancreatic Shock / Tom E. Ruud, Ansgar O. Aasen, Johan Pillgram-Larsen, and Jan O. Stadaas

Biological Availability of Injected or Aerosolized Alpha₁Proteinase Inhibitor / R.M. Smith, R.G. Spragg, and K.M. Moser

Multitherapy: A New Treatment Regimen in Endotoxemia / Ansgar O. Aasen, Tom E. Ruud, Johan Pillgram-Larsen, and Jan O. Stadaas

Hemodynamic Consequences of Multitherapy Pretreatment in Experimental Endotoxemia / J. Pillgram-Larsen, T.E. Ruud, J.O. Stadaas, and A.O. Aasen

1.3 Oxygen Radicals—Lipid Peroxidation

Oxygen Radicals and Lipid Peroxidation in Experimental Shock / Gerd O. Till and Peter A. Ward

Cytotoxic Lipid Peroxidation Products / Hermann Esterbauer, Ernst Koller, Peter Heckenast, Robert Moser, and Claude Celotto

Oxidant Injury of Cultured Cells: Biochemical Consequences / R.G. Spragg, I.U. Schraufstatter, P.A. Hyslop, D.B. Hinshaw, and C.G. Cochrane

Oxygen Radicals Scavenging in Prophylaxis and Treatment of Experimental Shock / G.P. Novelli, P. Angiolini, G. Martini, and R. Tani

Antioxidant Drugs and Shock Therapy / O. Orotolani, M. Biasiucci, A. Trebbi, M. Cianciulli, and R. Cuocolo

Protection by Ebselen Against Endotoxin Shock in Rats or Mice Sensitized by Galactosamine / K.-H. Konz, G. Tiegs, and A. Wendel

1.4 Prostaglandins, Leukotrienes, and Platelet Activation Factor

Activation of the Pulmonary Arachidonic Acid System and Its Consequences for Hemodynamics and Fluid Balance / Heinz Neuhofer, Werner Seeger, and Norbert Suttrop

Leukotrienes as Mediators in Endotoxin Shock and Tissue Trauma / Dietrich Keppler, Wolfgang Hagmann, and Claudio Denzlinger

Generation of Leukotrienes in Polytraumatic Patients With Adult Respiratory Distress Syndrome (ARDS) / J. Knöller, W. Schönfeld, T. Joka, J. Sturm, and W. König

On the Pathogenesis of Adult Respiratory Distress Syndrome—The Role of Anaphylatoxins, Leukotrienes and Platelet Activating Factor / U. Pison, K.P. Schmit-Neuerburg, and W. König

Increased Hemodynamic and Survival With Endotoxin and Septic Shock With Ibuprofen Treatment / Roger C. Bone, Elizabeth Rogers Jacobs, and Frank J. Wilson, Jr.

Effect of Ibuprofen on Components of an Acute Systemic Inflammatory Response Evoked by Intravenous Endotoxin Administration in the Conscious Sheep / Gary J. Jesmok, Frederick Aono, Janet Simpson, and Julian Borgia

Effect of the Nonsteroidal Antiinflammatory Agent BW755C in Rat and Sheep Endotoxemia / Soheyl Bahrami, Fred Mihm, Martin Thurnher, Christa Vogl, Anna Schiesser, Heinz Redl, and Günther Schlag

Effectiveness of Prostaglandin E₁ in Adult Respiratory Distress Syndrome / William C. Shoemaker

Efficiency of Prostacyclin in Rabbit Endotoxin Shock / Heinrich Ditter, Peter Röttger, Reinhard Voss, and F. Reinhard Matthias

1.5 Endotoxin

Endotoxin: The Causative Factor of Mediator Release During Sepsis / Daniel L. Traber

Endotoxin Shock Model in the Dog: A Reevaluation / Jean-Louis Vincent, Marc Domb, Pascal Luybaert, Corinne De Boelpaep, Philippe Van der Linden, and Serge Blécic

Perturbation of Transmembrane Signaling Mechanisms in Acute and Chronic Endotoxemia / Judy A. Spitzer, Elena R. Turco, Ion V. Deaciu, and Bryan L. Roth

Endotoxin-Induced Generation of Oxygen Free Radicals in Freshly Drawn Human Blood / Hubert Reichle, Dagmar Langner, Peter Wendt, and Günther Blümel

Inhibition of Lipopolysaccharide-Mediated Activation of Neutrophils With Monosaccharide Derivatives of Lipid A / Charles Lam, Elizabeth Basalka, Eberhard Schütze, and Hubert Walzl

2. RESULTS OF MEDIATOR RELEASE

Physiologic and Metabolic Correlations in Human Septic Shock / John H. Siegel

Multisystem Organ Failure / Hans-Peter Schuster

Changes in Metabolic Control in Injury and Sepsis / Rod A. Little and Keith N. Frayn

Catecholamines in the Serum of Multiple Trauma Patients—Mediators of ARDS? / P. Sefrin

Increased Systemic Microvascular Permeability in Septic Shock / A.B. Johan Groeneveld and Lambertus G. Thijs

Differences in Regional Oxygen Supply, Oxygen Consumption and Blood Flow During the Onset of E. coli Sepsis / G.I.J.M. Beerhuizen, R.J.A. Goris, H.J.M. Beijer, and G.A. Charbon
Vascular Perfusion of the Ischemic Small Intestine / Miklós Juhász, János Hamar, László Dézsi, Erzsébet Fehér, and Joachim Lutz

Reaction Pattern of Alveolar Cells in the Posttraumatic Lung Failure / Theo Joka, Udo Obertacke, Wolfgang Schönfeld, Susanne Oberste-Beulmann, Ulrich Pison, Ernst Kreuzfelder, Marianne Jochum, and Gerda Zilow

Phospholipid Lung Profile in Adult Respiratory Distress Syndrome—Evidence for Surfactant Abnormality / U. Pison, E. Gono, T. Joka, and U. Obertacke

Wound Inflammatory Mediators and Multisystem Organ Failure / Robert H. Demling

Burn Shock and Its Resuscitation / David N. Herndon, James G. Hilton, Daniel L. Traber, and Robert E. Barrow.

3. THE HEART AS A SPECIAL TARGET ORGAN IN SHOCK

Evaluation of Heart Performance With Special Emphasis on Severe Hemodynamic Changes During Hypovolemic-Traumatic Shock / Peter Krösl and Günther Schlag

Myocardial Dysfunction in Sepsis / John J. Spitzer, Lani W. Smith, Edmund C. Burke, and Kathleen H. McDonough

Studies on Low Molecular Weight Inotropic Plasma Substances in Prolonged Hypovolemic Traumatic Shock / Seth Hallström, Christa Vogl, Peter Krösl, Heinz Redl, and Günther Schlag

Cardiodepressant and Cardiostimulant Factors in Shock / Sandor Nagy

Release of Myocardial Depressant Factor (MDF) During Cardiopulmonary Bypass (CPB): Influence of Corticosteroids (Methylprednisolone) and Protease Inhibitor (Aprotinin) / Farag I. Coraim, Günther Laufer, Wilfried Ilias, Gregor Wollenek, and Ernst Wolner

Endogenous Nickel Release in Injured Patients: A Possible Cause of Myocardial Damage / Kornél Szabó, István Balogh, and Anna Gergely

Heart Rate During Hypotensive Central Hypovolemia Before and After Atropine in Man / Kåre Sander-Jensen, Jesper Mehlsen, Carsten Stædeager, Peter Bie, and Jørgen Warberg

Antioxidant Protection Against Free Radicals Mediated Myocardial Injury / Elizabeth Röth, Bela Török, William Bär, and Susan Pollak

Quantification of Granulocyte Enzymes/Proteins with Immunoassays

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This presentation provides the analytical background for the data of many experimental and clinical studies presented during the symposium, which are concerned with the role of neutrophil activation in the pathogenesis of shock. Figure 1 shows in a schematic way the events leading to, and produced by the activation of neutrophils. The proteolytic and oxidative action of neutrophil products, when released in excess of the local inhibitor concentrations, is one of the pathogenetic mechanisms in development of organ failure ultimately leading to shock.

We have developed immunoassays for 3 lysosomal proteins from the neutrophil;

- Elastase from the azurophilic granules, a neutral proteinase of very broad substrate specificity,
- Myeloperoxidase, also from the azurophilic granules, an enzyme involved in the oxidative activity of the neutrophil,

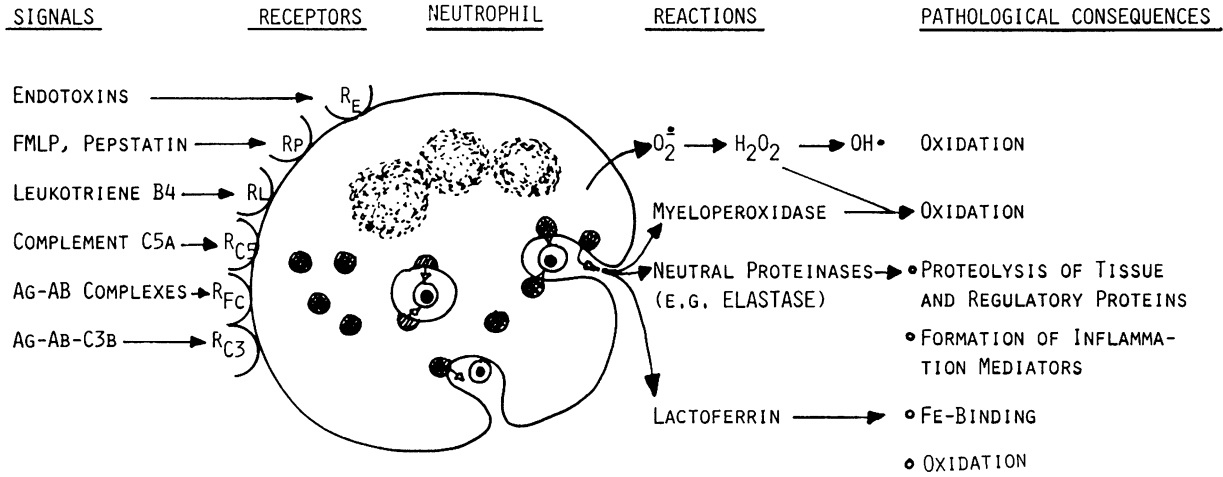


Figure 1

The Biochemistry of Neutrophil Activation

- Lactoferrin from the specific granules, an iron-binding protein, also involved in the oxidative mechanisms.

The assay principle of the tests is summarized in Figure 2. All assays are double antibody, solid phase, enzyme immuno assays. The marker enzyme is alkaline phosphatase. A special case is the elastase assay. PMN-elastase occurs in the blood in form of it's complex with α_1 -proteinase inhibitor. The analyte measured, therefore, is the elastase- α_1 -proteinase-inhibitor complex. The first antibody is directed against the enzyme, the second antibody against the inhibitor.

Not all of the elastase is bound to α_1 -proteinase inhibitor. As shown in Figure 3, in human blood about 90 % of elastase is bound to α_1 -proteinase inhibitor, and about 10 % to α_2 -macroglobulin. The elastase- α_2 -macroglobulin complex has a half life of only 10 minutes, whereas the elastase- α_1 -proteinase-inhibitor complex has a half life of about 1 hour. The analytical error inflicted by measuring only the fraction of elastase bound to α_1 -proteinase inhibitor, is negligible, therefore.

Details of the assay procedures for elastase-complex, myeloperoxidase, and lactoferrin are summarized in Table 1. The assay characteristics are given in Table 2, including the concentration of these proteins in the plasma of healthy human subjects (reference range).

The assays described are in the process of extensive evaluation of their usefulness as biochemical "Shock Predictors".

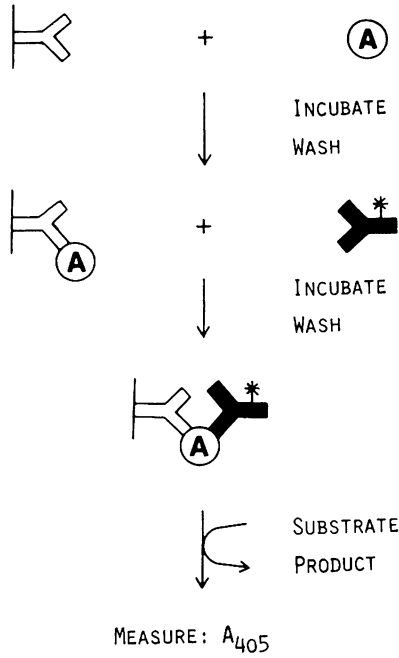
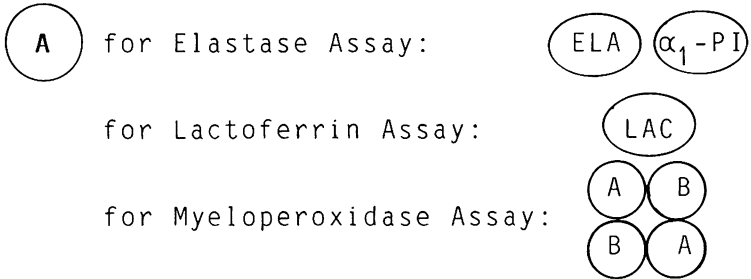


Figure 2

Assay Principle for Elastase, Myeloperoxidase, and Lactoferrin Immuno Assays



* Alkaline Phosphatase

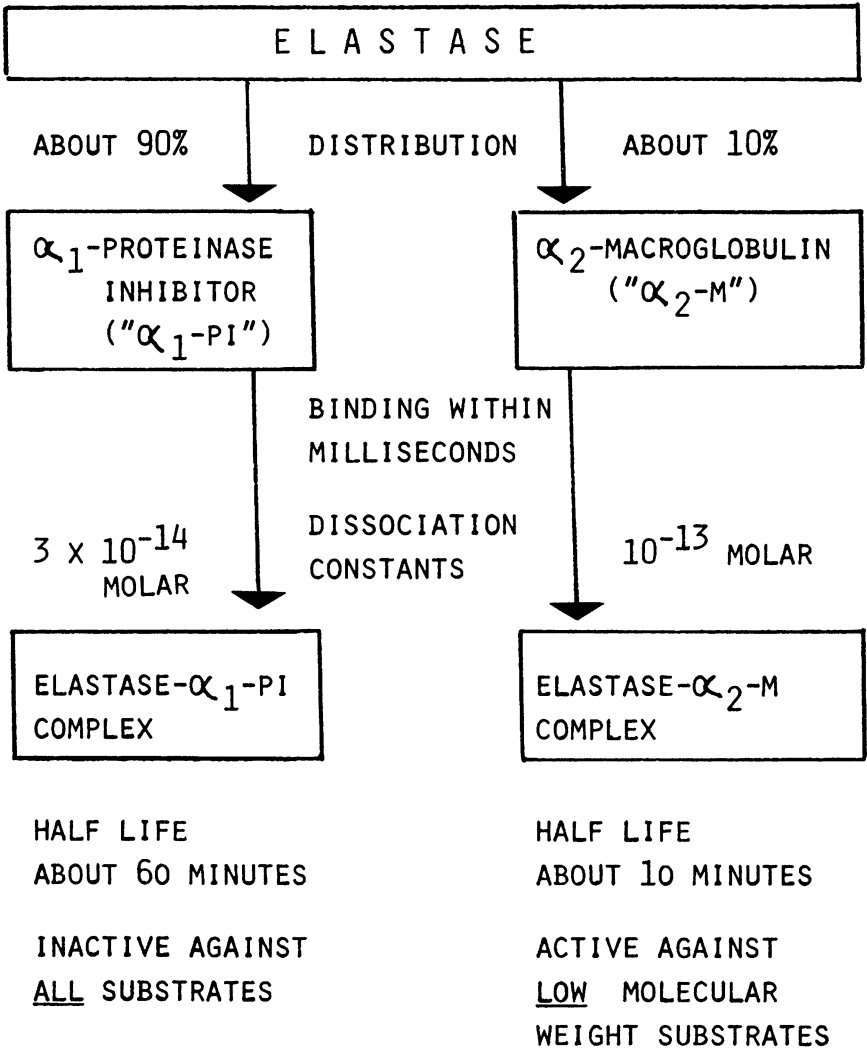


Figure 3

PMN Elastase and Inhibitor Systems in Blood

TABLE 1. A S S A Y P R O C E D U R E

	<u>ELASTASE COMPLEX</u>	<u>MYELOPEROXIDASE</u>	<u>LACTOFERRIN</u>
ASSAY TYPE	TWO-SITE ELISA	ELISA	ELISA
SOLID-PHASE ANTIBODY	A-ELASTASE	A-MYELOPEROXIDASE	A-LACTOFERRIN
SAMPLE DILUTION	1:51	1:21	1:50
INCUBATION TIME 1 (HR)	1	1	2
WASHING STEPS	3	3	3
CONJUGATE	A- α_1 -PI-AP	A-MPO-AP	A-LAC-AP
INCUBATION TIME 2 (HR)	1	2	2
WASHING STEPS	2	2	3
SUBSTRATE	- - - - P-NITROPHENYL PHOSPHATE - - - - -		
INCUBATION TIME 3 (HR)	1.5	1	1
REACTION VOLUME (ML)	0.5	0.5	0.5
INCUBATION TEMPERATURE	RT	RT	RT

ABBREVIATIONS: ELISA = ENZYME LINKED IMMUNOSORBENT ASSAY
 α_1 -PI = α_1 -PROTEINASE INHIBITOR (EX " α_1 -ANTI TRYPSIN")
MPO = MYELOPEROXIDASE
LAC = LACTOFERRIN
AP = ALKALINE PHOSPHATASE

TABLE 2. ASSAY CHARACTERISTICS

	<u>ELASTASE COMPLEX</u>	<u>MYELOPEROXIDASE</u>	<u>LACTOFERRIN</u>
<u>STANDARD CURVE</u>	0 - 10 µg/L	0 - 20 µg/L	0 - 10 µg/L
<u>CALIBRATION CURVE:</u> <u>CALCULATION</u>	LINEAR REGRESSION	LINEAR REGRESSION	LINEAR REGRESSION
<u>DETECTION LIMIT</u> (BLANK + 3 SD)	0,25 µg/L	0,25 µg/L	0,25 µg/L
<u>SAMPLES:</u>			
SERUM	∅	∅	+
EDTA PLASMA	+	+	+
CITRATE PLASMA	+	+	+
<u>IMPRECISION:</u>			
WITHIN-RUN (%)	4 - 8 (N=10)	7 - 9 (N=15)	2 - 5 (N=10)
BETWEEN-RUN(%)	3 - 8 (N=10)	5 -12 (N= 9)	4 -10 (N=10)
<u>REFERENCE RANGE</u> (MEAN ± S.D.) IN CITRATE PLASMA	67 ± 29 µg/L	36 ± 12 µg/L	137 ± 51 µg/L

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