



# Thrombelastography

*By*

PIETRO DE NICOLA

*Associate Professor  
Department of Medicine  
University of Pavia  
Italy*



CHARLES C THOMAS • PUBLISHER

*Springfield • Illinois • U.S.A.*

CHARLES C THOMAS • PUBLISHER  
BANNERSTONE HOUSE  
301-327 East Lawrence Avenue, Springfield, Illinois, U.S.A.

*Published simultaneously in the British Commonwealth of Nations by*  
BLACKWELL SCIENTIFIC PUBLICATIONS, LTD., OXFORD, ENGLAND

*Published simultaneously in Canada by*  
THE RYERSON PRESS, TORONTO

This book is protected by copyright. No part  
of it may be reproduced in any manner with-  
out written permission from the publisher.

*Copyright 1957, by* CHARLES C THOMAS • PUBLISHER

Library of Congress Catalog Card Number: 57-10430

*Printed in the United States of America*

## THROMBELASTOGRAPHY

*Publication Number 316*

AMERICAN LECTURE SERIES®

*A Monograph in*

AMERICAN LECTURES IN PHARMACOLOGY

*Edited by*

CHAUNCEY D. LEAKE, Ph.D.

*Pharmacology Laboratory*

*Ohio State University*

*Columbus, Ohio*

## FOREWORD

IT is a pleasure for me to present again to the American readers a work of Dr. Pietro de Nicola, which is to be published in the beautiful American Lecture Series by Charles C Thomas. This volume on thrombelastography should be considered as a monographic follow-up of the previous work on the diagnosis of coagulation defects. Much attention has been given during the last few years to thrombelastography, which is certainly a useful tool for blood coagulation studies both from the scientific and diagnostic point of view. The knowledge on this field is now rather crystallized, and, although several interpretative problems are still awaiting an answer, the clinical significance of thrombelastography seems to be quite established. At the time of the first Symposium on thrombelastography, held in Pavia in 1954, the topic appeared to be reserved to a few specialists, or rather pioneers. Now, this method of research is almost indispensable for our routine diagnostic work, and we feel quite happy to be among the first ones who used it.

Dr. de Nicola succeeded in assembling in this volume most of his experience on this field and to give a general outline of the actual possibilities of thrombelastography in clinical investigations. He is certainly very much qualified for such a task, insofar as his basic knowledge on the blood coagulation mechanisms allowed him to properly interpret the thrombelastographic data. As far as thrombelastography is concerned, we are now at approxi-

mately the same stage of evolution as electrocardiography several years ago. It is among my best wishes that the same luck be encountered by thrombelastography in a short time. In the meanwhile, I wish a full success to the present work, which deserves high appreciation and will contribute to the wide diffusion of the new method.

PAOLO INTROZZI  
Professor of Medicine  
University of Pavia  
Pavia, Italy

## PREFACE

THE PURPOSE of this work is to give a concise outline of the biologic and clinical significance of thrombelastography, on the basis of personal investigations. The material presented is derived from researches carried out during the last three years in the Clinica Medica of the University of Pavia, which are quoted in bibliography and also include full reference to other investigations in the same field. The pioneer and fundamental work of Dr. Hellmut Hartert, Heidelberg, Germany, should be here acknowledged, insofar as he first projected, during and after World War II, the new apparatus, which was then called a thrombelastograph. At the very beginning, his method was used only in a few German laboratories. During later years, a number of thrombelastographic units were operating in several European countries, and quite recently, also in the United States. An official recognition of the clinical importance of thrombelastography took place in Pavia, Italy, where the first international Symposium on thrombelastography was organized in 1954 by Professor Introzzi and was attended by the leading European workers in this field, headed by Dr. Hartert. It was felt that a summarizing publication might be useful to investigators and clinicians as a guide for a proper understanding of the new method, before a more comprehensive survey be presented on the basis of the experience collected in a number of laboratories.

Permission for reproducing some illustrations from



personal articles, was kindly given by the following journals: *The American Journal of Clinical Pathology*; the *American Journal of Roentgenology*; *Radium Therapy and Nuclear Medicine*; *Blood*; *Blut*; *Deutsches Archiv für Klinische Medizin*, and *Sang*.

Advice and suggestions for our work on thrombelastography and the preparation of the manuscript were generously and liberally given to us by Dr. Hartert, whose encouragement and help are here gratefully acknowledged. His friendly and pertinent cooperation in this connection resulted in a fruitful development of the several problems which were encountered during our investigations.

P.D.N.

## CONTENTS

	<i>Page</i>
<i>Foreword</i> . . . . .	v
<i>Preface</i> . . . . .	vii
 <i>Chapter</i>	
I. INTRODUCTION . . . . .	3
II. THROMBELASTOGRAPHY . . . . .	5
Description of the Apparatus . . . . .	6
Thrombelastographic Technique . . . . .	11
The Normal Thrombelastogram . . . . .	14
The Thrombelastogram in Various Mammals . . . . .	25
III. THE HEMOPHILIC SYNDROMES . . . . .	28
Thrombelastographic Characteristics in Hemophilic Syndromes . . . . .	28
Thrombelastographic Findings in Hemophilic Syndromes after Blood and Plasma Transfusion . . . . .	30
IV. THE PLATELET DEFICIENCIES . . . . .	33
Thrombelastographic Characteristics of Platelet-free Plasma . . . . .	33
Thrombelastographic Characteristics of Platelet Deficiencies . . . . .	35
The Effect of Splenectomy on Thrombelastogram in Thrombocytopenic Patients . . . . .	40
The Effect of X-rays on Thrombelastogram . . . . .	41

	<i>Page</i>
The Addition of Platelets from Thrombocytopenic Subjects to Platelet-poor Plasma .....	42
V. PROTHROMBIN, FACTOR VII AND AC-GLOBULIN DEFICIENCIES .....	45
The Isolated Deficiencies of Prothrombin, Ac-Globulin and Factor VII .....	45
The Combined Deficiencies of Prothrombin, Ac-Globulin and Factor VII .....	47
VI. THROMBELASTOGRAPHIC STUDY OF FIBRINOLYSIS....	49
The Study of Spontaneous Fibrinolysis .....	49
The Streptokinase Activated Fibrinolysis .....	50
VII. THROMBELASTOGRAPHIC ANALYSIS OF THROMBO- PHILIC CONDITIONS .....	64
Introduction .....	64
Experimentally Produced Thrombophilic Condi- tions .....	64
The Thrombelastographic Characteristics of Thrombophilic Conditions in Clinical Ob- servations .....	66
VIII. THE INFLUENCE OF SOME DRUGS ON THE THROM- BELASTOGRAM .....	76
Heparin and Heparin-Like Substances .....	76
Coumarine and Indanedione Derivatives .....	81
Antimitotics and Antimetabolites .....	85
The Action of Dextran In Virto and In Vivo.....	90
Vitamin E .....	96
Magnesium Compounds .....	97
Fatty Meals .....	100
IX. CONCLUSIONS .....	102
References .....	105
Index .....	109

## THROMBELASTOGRAPHY



# I

## INTRODUCTION

THE QUANTITATIVE evaluation of physicochemical modifications during the transformation of fibrinogen into fibrin has permitted the elaboration of various methods for the study of coagulation and the recognition of alterations in physiopathologic conditions.

A general evaluation of the methods based on physicochemical modifications was attempted in the past, on the basis of the following factors: 1) electrical resistance; 2) viscosity; 3) transparency; 4) colloidal gold (modifications of the protecting power of proteins); 5) pH. The usual methods are based on modifications in viscosity and transparency. Recently, however, improved diagnostic methods have been proposed.

The methods based on modifications in transparency are optical. Microscopical methods, and, in general, all methods based on morphological changes (roentgenspectrography and, above all, the electron microscope) are also optical, but not always practical. In the study of changes in transparency, it is necessary to use plasma because the corpuscles hinder correct observation.

Methods based on changes in viscosity are more commonly employed. The most simple methods used in the determination of the coagulation time of whole blood belong to this group. Since the transformation of fibrinogen into fibrin always corresponds to an increase in viscosity, any of the above mentioned procedures will permit the following of the variations in viscosity with more or

less precision. This is valid for both direct and indirect methods of viscosimetry, based on the use of machines at times very complicated or on relatively simple procedures.

The hemostatic action of the clot is not only related to changes in the viscosity, i.e., with the conversion of fibrinogen from a sol to a gel, but also to changes in the structure and organization of the molecules of fibrin according to determined laws. In structural modifications, one encounters the development of an elastic force that may represent the most significant characteristic of the clot and may also be related to its hemostatic function.

## II

### THROMBELASTOGRAPHY

THE RECENT method proposed for the measurement of the elasticity of a clot, or thrombelastography, represents an improvement in respect to the preceding methods. It permits the measurement of changes in viscosity and elastic properties of the clot during the whole coagulation process under conditions that are constant and reproducible. It, therefore, allows one to follow the whole process of coagulation from its beginning to the dissolution of the clot or fibrinolysis. By means of thrombelastography, it is also possible to obtain a graphic registration of these variations and thus give an objective and permanent documentation of the coagulation of blood in its various phases.

The principle used in the elaboration of the thrombelastographic method is the following. To measure the elasticity of the clot, it is necessary to bear in mind the deformation of the clot, and in particular, the force and amount of deformation. This is not possible if, immediately after the onset of coagulation, the clot retracts from the surface of the measuring apparatus. In order to avoid this inconvenience, the clot is made to adhere to the surface of the container. From previous research it was noted that highly levigated surfaces could obtain this result. However, under such conditions, the traction of the fibrin threads must be relatively small so as not to determine irreversible alterations in the fibrin network. On the other hand the traction force must be a specific



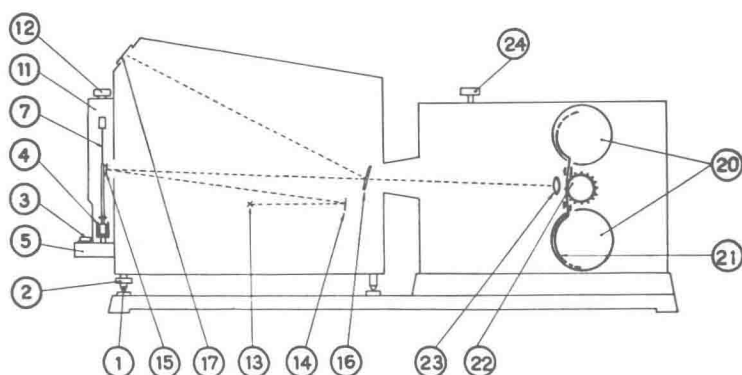


Figure 1. Thrombelastograph; longitudinal section.

expression of the clot elasticity, thus avoiding the intrinsic variations in viscosity and correlating deformation to time. Finally, the traction must be uniform in every direction and completely without friction.

In thrombelastography, these requirements were realized and permit an exact measurement of the elasticity during the course of coagulation. It also permits the simultaneous or separate analysis of several (usually three) blood samples. These advantages allow the thrombelastogram to be used in the routine work up of coagulation disorders.

### DESCRIPTION OF THE APPARATUS

Schematically, the apparatus is constructed so as to obtain the graphic registration of the movements of a steel wire under constant experimental conditions, and particularly at a constant temperature and with uniform movements of the container.

The apparatus is divided into two parts, the thrombelastograph itself and the kymograph (Figure 1). These two parts are contained in a single light-tight housing and are mounted on a shelf which is connected to the labora-