

Nitrates III

Cardiovascular Effects

Edited by

P.R. Lichtlen H.-J. Engel

A. Schrey H.J.C. Swan



Springer-Verlag
Berlin Heidelberg New York

Nitrates III

Cardiovascular Effects

Edited by

P. R. Lichtlen H.-J. Engel

A. Schrey H. J. C. Swan

With 326 Figures

Springer-Verlag
Berlin Heidelberg New York 1981

Professor Dr. P. R. LICHTLEN
Med. Hochschule Hannover Abteilung für Kardiologie
Karl-Wiechert-Allee 9, D-3000 Hannover 61

Priv.-Doz. Dr. H.-J. ENGEL
Zentralkrankenhaus „Links der Weser“,
Senator-Weßling-Straße, D-2800 Bremen 61

Dr. A. SCHREY
Pharma-Schwarz GmbH, D-4019 Monheim

Dr. H. J. C. SWAN
Director, Dept. of Cardiology Cedars-Sinai Medical Center
8700 Beverly Boulevard, Los Angeles, Calif. 90048, USA

ISBN 3-540-10761-4 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-10761-4 Springer-Verlag New York Heidelberg Berlin

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machine or similar means, and storage in data banks. Under § 54 of the German Copyright Law where copies are made for other than private use, a fee is payable to 'Verwertungsgesellschaft Wort', Munich.

© by Springer-Verlag Berlin Heidelberg 1981
Printed in Germany.

The use of registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Typesetting, Offsetprinting and Binding: Brühlsche Universitätsdruckerei Giessen
2121/3130-543210

Preface

Pharmacological and clinical research on nitrates continues to be of growing interest in many centers. This is surprising in view of the fact that their favorable effects in angina pectoris were described by Brunton and by Murrell in the *Lancet* more than 100 years ago.

As expected, a host of new information has been collected since the two previous symposia on nitrates held in Stockholm in 1975 and Berlin in 1978. New insights were gained into the pharmacology, pharmacokinetics and pharmacodynamics of nitrates, as well as into their clinical effects in acute and chronic ischemic heart diseases and in severe congestive heart failure. Relatively little progress, however, was observed in research into the basic action of nitrates. Although most investigators agree that intracellular sequestration of calcium is probably the main mechanism by which nitrates lead to the reduction of vascular smooth muscle tone, the exact site of their action still remains undefined. In contrast, dose-dependent differences in venous and arteriolar tone have long been clearly established.

Treatment was again in the main stream of discussion. The question of tolerance following long-term administration was discussed in depth and the term "pseudotolerance" was introduced to describe the adaptation of the body's circulatory system to chronic vasodilation. This is especially important in long term prophylactic antiischemic treatment in stable, as well as in unstable angina pectoris (i.e. during increased vasomotor tone – spasm).

The editors and organizers of the meeting wish to express their thanks not only to the sponsors, but especially to those active participants from all over the world who once again demonstrated the true spirit of a scientific community in the search for ever more knowledge on the therapeutic effects of one of the oldest, though still most potent drugs in the cardiovascular field.

The Editors

List of Active Participants

A. L'ABBATE

Laboratorio del Consiglio
Nazionale delle Ricerche
presso l'Università
Via G. Savi 8
I-56100 Pisa

K. VAN ACKERN

Med. Klinik I
Klinikum Großhadern
Marchioninistraße 15
D-8000 München 70

I. AMENDE

Med. Hochschule Hannover
Department für Innere Medizin
Abt. für Kardiologie
Karl-Wiechert-Allee 9
D-3000 Hannover 61

E. ANJOU

Department Clinical Physiology
Thoracic Hospital
S-10401 Stockholm

N. A. AWAN

Heart Failure Laboratory
Section of Cardiovascular Medicine
University of California
Davis, California 95616, USA

R. BALCON

The London Chest Hospital
Bonner Road, E2, 9JX
GB-London

S. BALIGADOO

Route de St. Paul
Vacoas, Mauritius

E. BASSENCE

Lehrstuhl für Angew. Physiologie
der Universität
Hermann-Herder-Straße 7
D-7800 Freiburg i. Br.

A. H. BECKETT

Department of Pharmacy
Chelsea College
University of London
Manresa Road
GB-London SW3 6LX

W. BLEIFELD

Kardiolog. Abteilung
Univ.-Krankenhaus Eppendorf
II. Med. Klinik
Martinistraße 22
D-2000 Hamburg 20

M. G. BOGAERT

c/o Heymans Inst. für Pharmakologie
Universität Gent
De Pintelaan 135
B-9000 Gent

J. BONNIER

Catharina Ziekenhuis
Michelangelolaan 2
NL-Eindhoven

S. BONORON-ADÈLE

Unité 8 I.N.S.E.R.M.
de Recherches de Cardiologie
Avenue du Haut-Léveque
F-33600 Pessac

J. BORER
New York Hospital-Cornell University
Medical Center
525 East 68th Street
New York, New York 10021, USA

J.-P. BROUSTET
Hopital Cardiologique
du Haut Léveque
Av. de Magellan
F-33604 Pessac

D. BRUNNER
Donolo Institute of
Physiol. Hygiene
P.O. Box 8093
IL-Jaffa

W.-D. BUSSMANN
Zentrum der Inneren Medizin
Klinikum der Universität
Theodor-Stern-Kai 7
D-6000 Frankfurt/M. 70

L. P. CHASSEAUD
Department of Metabolism
& Pharmacokinetics
Huntingdon Research-Centre
GB-Huntingdon, Cambs PE18 6ES

F. CHICHE
Service de Cardiologie
et Urgences Circulatoires
Hopital Tenon
4, Rue de la Chine
F-75970 Paris Cedex 20

J. N. COHN
Cardiovascular Division
University of Minnesota-Med. School
Veterans Administration Hospital
54, Street and 48th Avenue South
Minneapolis, Minnesota 55455, USA

S. R. CONTI
Division of Cardiology
University of Florida
Box J. 277, JHM Health Center
Gainesville, Florida 32610, USA

P. DEEG
Med. Universitätsklinik
Abt. Kardiologie
I.-Schneider-Straße 5
D-8700 Würzburg

H. DENOLIN
178, avenue Winston Churchill
B-1180 Bruxelles

A. DISTANTE
c/o Laboratorio del Consiglio
Nazionale delle Ricerche
presso l'Università
degli Studi di Pisa
Via G. Savi 8
I-56100 Pisa

W. DOERING
Krankenhaus München-Schwabing
II. Medizinische Abteilung
Kölner Platz 1
D-8000 München 40

W. H. DOWN
Huntingdon Research Centre
GB-Huntingdon, Cambs PE18 6ES

V. DRAXLER
Allgemeines Krankenhaus
Klinik für Anästhesie und Allgemeine
Intensivmedizin der Universität Wien
Spitalgasse 23
A-1090 Wien

H.-J. ENGEL
Zentralkrankenhaus „Links der Weser“
Senator-Weßling-Straße
D-2800 Bremen 61

J. T. FLAHERTY
The Johns Hopkins Medical Institute
Baltimore, Maryland 21205, USA

J. A. FRANCIOSA
Veteran Administration Hospital
Philadelphia, PA 19104, USA

H. L. FUNG
State University of New York
at Buffalo
Department of Pharmaceutics
517 Hochstetter Hall
Buffalo, New York 14260, USA

W. GANZ
Cedars Sinai Medical Center
8700 Beverly Boulevard
Los Angeles, Calif. 90084, USA

J. A. GASCHO
Cardiovascular Center
The University of Iowa
Hospitals and Clinics
Iowa City, Iowa, USA

L. S. GEISLER
Innere Abteilung des
St. Barbara-Hospital
D-4390 Gladbeck

L. GEORGIEW
Zentrum für Kardiologie
III. Städt. Krankenhaus
Miko-Papostz 65
Sofia, Bulgarien

U. GLEICHMANN
Gollwitzer-Meyer-Institut
Klinik für Herz- und
Kreislaufkrankungen
Herforder Straße 43
D-4970 Bad Oeynhausen

A. GRÜNTZIG
Emory University
School of Medicine
1364 Clifton Road
Atlanta, Georgia 30322, USA

H. W. HEISS
Medizinische Klinik
Universität Freiburg
Hugstetter Straße 55
D-7800 Freiburg i. Br.

A. HOLMGREN
Karolinska Sjukhuset
Fach 10401
S-60500 Stockholm

W. HOMBACH
Medizinische Klinik und Poliklinik
der Universität Köln
Abteilung f. Kardiologie
Josef-Stelzmann-Straße 9
D-5000 Köln 41

V. HOSSMANN
II. Med. Klinik
Krankenhaus Merheim
Ostmerheimer Straße 200
D-5000 Köln 91

P. G. HUGENHOLTZ
Dept. of Cardiology
Thoraxcenter P.O. Box 1738
NL-Rotterdam

P. IMHOF
Ciba Geigy Ltd.
Research Department
Pharmaceuticals Division
CH-4002 Basel

W. JANSEN
III. Med. Universitätsklinik und
Poliklinik Köln
Lehrstuhl für Innere Medizin III
Josef-Stelzmann-Straße 9
D-5000 Köln 41

H. JUST
Med. Univ.-Klinik
Hugstetter Straße 55
D-7800 Freiburg i. Br.

F. KAINDL
Universitätsklinik
Abteilung f. Kardiologie
Allgem. Krankenhaus der Stadt Wien
Garnisonsgasse 13
A-Wien

M. KALTENBACH
Abteilung für Kardiologie
Zentrum der Inneren Medizin
Klinikum der Universität
Theodor-Stern-Kai 7
D-6000 Frankfurt/M. 70

W. KLEIN
Med. Universitätsklinik
Aunbruggerplatz 15
A-8036 Graz

G. KOBER
Klinikum d. J. W. Goethe-Univ.
Zentrum der Inneren Medizin
Abteilung Kardiologie
Theodor-Stern-Kai 7
D-6000 Frankfurt/M. 70

H. P. KRAYENBÜHL
Med. Poliklinik
der Universität
Kantonsspital
CH-8006 Zürich

H. KREUZER
Kardiologische Univ.-Klinik
Neuklinikum der Universität
Robert-Koch-Straße 40
D-3400 Göttingen

V. KREYE
II. Physiologisches Institut
Universität Heidelberg
Im Neuenheimer Feld 326
D-6900 Heidelberg

W. KÜBLER
Med. Universitätsklinik
– Abt. III – Kardiologie –
Klinikum der Universität
Bergheimer Straße 58
D-6900 Heidelberg

P. R. LICHTLEN
Med. Hochschule Hannover
Abt. für Kardiologie
Karl-Wiechert-Allee 9
D-3000 Hannover 61

F. LOOGEN
I. Med. Klinik B
Abteilung f. Kardiologie
Moorenstraße 5
D-4000 Düsseldorf 1

J. A. MANTLE
The University of Alabama
Birmingham – Medical Center
Birmingham, Alabama 35294, USA

D. T. MASON
Chief Cardiovascular Medicine
University of California
Davis, Calif. 95616, USA

H. MATTHYS
Klinikum der Albert-Ludwigs-Univ.
Med. Universitätsklinik
Abt. Pulmologie
D-7800 Freiburg i. Br.

H. G. MEHMEL
Med. Universitätsklinik
Abt. III, Kardiologie
Bergheimer Straße 58
D-6900 Heidelberg 1

W. MERX
Innere Medizin I
d. Rhein.-Westf. Techn. Hochschule
Goethestraße 27–29
D-5100 Aachen

H. N. NEUFELD
Heart Institute
Tel Hashomer Medical Center
IL-Tel Aviv

B. NIEHUES
Med. Klinik und Poliklinik
Lehrstuhl Innere Medizin III
Abt. f. Kardiologie der
Universität Köln
Josef-Stelzmann-Str. 9
D-5000 Köln 41

A. PAGE
Hôpital Cardiologique
Avenue du Haut-Levéque
F-33604 Pessac

M. PANTZER
c/o Bernische Höhenklinik
CH-3625 Heiligenschwendi

J. O. PARKER

Etherington Hall
Queen's University
Kingston, Ontario
Canada

W. W. PARMLEY

Division of Cardiology
Chief Cardiovascular Medicine
University of California
1186 Moffitt
San Francisco, Calif. 94143, USA

TH. PASCH

Institut für Anaesthesiologie
Univ.-Krankenhaus Erlangen
D-8520 Erlangen

B. PITT

University of Michigan
Dept. of Medicine
Div. of Cardiology
24th East Ridge Way
Ann Arbor, Mich. 48104, USA

P. PROBST

Kardiologische Univ.-Klinik
Allgemeines Krankenhaus
der Stadt Wien
Garnisonsgasse 14
A-1097 Wien

B. RABINOWITZ

Coronary Care Unit
c/o Chaim Sheba Medical Center
IL-Tel Aviv

W. RAFFLENBEUL

Med. Hochschule Hannover
Dept. für Innere Medizin
Abt. für Kardiologie
Karl-Wiechert-Allee 9
D-3000 Hannover 61

P. RENTROP

Abteilung Kardiologie
Med. Klinik der
Universitätsklinik Göttingen
Robert-Koch-Straße 40
D-3400 Göttingen

A. RICKARDS

National Heart Hospital
Westmoreland Street
GB-London WIM 88A

M. ROTHLIN

Chirurgische Klinik A
Kantonsspital Zürich
CH-8091 Zürich

ST. RUBIN

Cedars-Sinai Medical Center
8700 Beverly Boulevard
Los Angeles, Calif. 90048, USA

W. RUDOLPH

Deutsches Herzzentrum
Lothstraße 11
D-8000 München 19

W. RUTSCH

Klinikum Charlottenburg der
Freien Universität Berlin
Abt. Innere Medizin – Kardiologie –
Spandauer Damm 130
D-1000 Berlin 19

G. SAUER

Med. Univ.-Klinik Göttingen
Abt. Kardiologie
Robert-Koch-Straße 40
D-3400 Göttingen

F. SEIDEL

c/o Stiftsklinik Augustinum
Innere Klinik
Stiftsbogen 74
D-8000 München 70

P. K. SHAH

Cedars Sinai Medical Center
8700 Beverly Boulevard
Los Angeles, Calif. 90048, USA

U. SIGWART

Centre Hospitalier
Universitaire Vaudois
CH-1011 Lausanne

H. SIMON

Med. Universitätsklinik Bonn
D-5300 Bonn-Venusberg

R. SIMON
Med. Hochschule Hannover
Abt. f. Kardiologie
Karl-Wiechert-Allee 9
D-3000 Hannover 61

V. F. SMOLEN
Ayerst Laboratories, Inc.
Rouses Point, N.Y. 12979, USA

H. J. C. SWAN
Dept. of Cardiology
Cedars-Sinai Medical Center
8700 Beverly Boulevard
Los Angeles, Calif. 90048, USA

M. SCHARTL
Klinikum Charlottenburg
der Freien Universität Berlin
Abt. Innere Medizin
– Kardiologie –
Spandauer Damm 130
D-1000 Berlin 19

A. SCHINZ
c/o Klinik Höhenried für Herz-
und Kreislauferkrankungen
der LVA Oberbayern
D-8131 Bernried

F. W. SCHMAHL
Zentrum für Innere Medizin
des Klinikums d. Just.-Liebig-Univ.
Klinikstraße 36
D-6300 Gießen

R. SCHRÖDER
Med. Klinik und Poliklinik
Klinikum Steglitz d. Freien Universität
Hindenburgdamm 30
D-1000 Berlin 45

M. STAUCH
Kardiolog. Abteilung der
Universität Ulm
Steinhövelstraße 9
D-7900 Ulm

B. STEGARU
c/o Städt. Kliniken Mannheim
– Kardiologie –
Postfach 23
D-6800 Mannheim 1

P. STÜRZENHOFECKER
Benedikt-Kreutz-Rehabilit.-Zentrum
f. Herz- und Kreislauferkrankungen
Südring 15
D-7812 Bad Krozingen

T. TAYLOR
c/o Huntingdon Research Center
GB-Huntingdon, Cambs. PE18 6ES

U. TEBBE
Med. Klinik der Universität
Abteilung für Kardiologie
Robert-Koch-Straße 40
D-3400 Göttingen

H. TILLMANN
Med. Univ.-Klinik Heidelberg
Innere Medizin
Abteilung III – Kardiologie
Bergheimer Straße 58
D-6900 Heidelberg 1

H. TYDÉN
Department of Anaesthesiology
University Hospital
S-75014 Uppsala

H. WEBER
Klinikum Charlottenburg der
Freien Universität Berlin
Abt. Innere Medizin – Kardiologie –
Spandauer Damm 130
D-1000 Berlin 19

K. W. WESTERMANN
Postfach 610 163
D-2000 Hamburg 61

M. M. WINBURY
Warner-Lambert-Laboratories
2800 Plymouth Road
Ann Arbor, Michigan 48109, USA

A. WIZEMANN
Universitätsklinik-Augenklinik
Friedrichstraße 18
D-6300 Gießen

R. WOLF
Römstedter Straße 25
D-3118 Bad Bevensen

Nitrates III Cardiovascular Effects

Contents

Part I Basic Action of Nitrates

Pharmacology of Nitrates in Relation to Antianginal Action. M. M. WINBURY	2
Pharmacokinetics – Pharmacodynamics and the Bioavailability of Organic Nitrate Drug Products. V. F. SMOLEN	12
Fate of Isosorbide Mononitrates in Man. M. G. BOGAERT, M. T. ROSSEEL, and O. TEIRLYNCK	23
Tolerance to Circulatory and Clinical Effects of Nitrates. J. O. PARKER and U. THADANI	27
Panel Discussion.	37

Part II Pharmacodynamics and Kinetics

Pharmacokinetics of Isosorbide Dinitrate in Human Subjects. T. TAYLOR and L. F. CHASSEAUD	40
Pharmacokinetics of Isosorbide Mononitrates in Human Subjects. L. F. CHASSEAUD and T. TAYLOR	47
Comparative Haemodynamic and Pharmacokinetic Investigations After Oral Isosorbide-2-mononitrate and Isosorbide-5-mononitrate. F. SEIDEL and D. MICHEL	54
Newer Methods of Administration of Nitrates to Man to Give a More Predictable Therapeutic Response. A. H. BECKETT	61
Plasma Concentrations and Hemodynamic Effects of Percutaneously Administered Nitroglycerin and Isosorbide Dinitrate in Healthy Volunteers. P. R. IMHOF, B. OTT, A. WEISS, L.-C. CHU, and L. F. CHASSEAUD	66
Effects of Acute and Chronic Administration of Isosorbide Dinitrate, Sustained-Release Form, in Patients with Angina Pectoris. W. RUDOLPH, R. BLASINI, K.-L. FROER, U. BRUEGMANN, A. MANNES, and D. HALL	75
May Prolonged High Doses of Nitrates Cause Tolerance? Preliminary Results on the Response to an Additional Dose by Infusion. A. DISTANTE, A. L'ABBATE, C. PALOMBO, C. MICHELASSI, D. ROVAI, M. A. MORALES, F. SABINO, E. MOSCARELLI, M. LOMBARDI, and A. MASERI	82

The New Tropical Drug Delivery System for Nitroglycerin. B. PITT, H. COLFER, A. KEITH, P. STETSON, J. WALTON, J. BRYMER, A. GOLUB, and B. LUCCHESI	91
Echocardiographic Assessment of Different Doses of Oral Isosorbide Dinitrate in Patients with and without Heart Failure: Increase in Response with Dose. S. BALIGADOO, J. P. DENIZEAU, P. BITAN, and P. CHICHE	95
Unchanged Efficacy of Acute Sublingual Nitrate Compounds During Long-term Treatment with Percutaneously Applied Isosorbide Dinitrate Ointment. D. BRUNNER, J. WEISBORD, N. MESHULAM, and S. MARGULIS.	100
Induction and Inhibition of Organic Nitrate Metabolism. W. H. DOWN, L. F. CHASSEAUD, and S. A. BALLARD	110
Digital Pulse Plethysmography: a Sensitive Test of the Pharmacodynamics of Nitrates – Reproducibility and Quantitation of the Technique. A. SCHINZ, A. GOTTSÄUNER, and K. SCHNELLE	117
Discussion	123

Part III Hemodynamics

Direct and Indirect Effects of Nitroglycerin on Systolic and Diastolic Left Ventricular Function. I. AMENDE, R. SIMON, W. P. HOOD Jr., W. DANIEL, and P. LICHTLEN	126
Left Ventricular Function and Regional Wall Motion After Intracoronary Application of Nitrates in Coronary Heart Disease. W. RUTSCH and H. SCHMUTZLER	134
Different Effects of Intracoronary and Intravenous Administration of Nitroglycerin on the Microcirculation of the Ventricular Myocardium of the Cat and Rat Heart. H. TILLMANN, M. STEINHAUSEN, H. LEINBERGER, H. THEDERAN, R. JAUERNIG, and W. KÜBLER	141
Diastolic Pressure-Volume Relation and Left Ventricular Mass in Man After Autonomic Blockade and During Afterload Variation with Isosorbide Dinitrate and Methoxamine. H. C. MEHMEL, K. RUFFMANN, K. V. OLSHAUSEN, G. SCHULER, F. SCHWARZ, and W. KÜBLER.	147
Early Hemodynamic Responses to Single Dose Intravenous Nitroglycerin: Time Course Relationships. C. R. CONTI, L. G. CHRISTIE Jr., W. W. NICHOLS, R. L. FELDMAN, C. J. PEPINE, and J. MEHTA.	151
Demonstration of a Real Inotropic Effect of Nitrites on Myocardial Contractility During Anoxia and Reoxygenation: Attempt to Determine Action Site with the Contribution of Calcium Antagonistic Compounds. S. BONORON- ADÈLE, L. TARIOSE, H. BRICAUD, and P. BESSE	157
Use of Intravenously Administered Isosorbide Dinitrate to Determine Reversibility of Myocardial Asynergy After Myocardial Infarction. J. J. R. M. BONNIER and M. EL GAMAL	170

Hemodynamic Interaction of Beta-Blockers and Nitrates in Coronary Heart Disease. W. DOERING, H. HACKER, W. REISER, and E. KÖNIG	175
Discussion	180

Part IV Coronary Flow, Perfusion

Effect of Nitrates on Myocardial Blood Flow During Angina: Comparison of Results Obtained by Inert Gas Clearance and 201 Thallium Imaging. H.-J. ENGEL, R. WOLF, P. PRETSCHNER, H. HUNDESHAGEN, and P. R. LICHTLEN	184
Collateral Pressure Distal to Coronary Obstructions – Influence of Nitrates. A. GRÜNTZIG	192
Effects of Systemic Nitroglycerin on Perfusion of Ischemic Myocardium in Clinical Coronary Artery Disease. D. T. MASON, R. C. KLEIN, and N. A. AWAN	193
Effects of Nitroglycerin on Blood Velocity and Flow in Coronary Arteries and Bypass Grafts in Man. R. SIMON, I. AMENDE, and P. R. LICHTLEN	202
The Effect of Nitrates on Pressure-time Indices and Coronary Graft Blood Flow in Man. R. M. DONALDSON and A. F. RICKARDS	209
Angina Pectoris and Other Effects After Intracoronary Administration of Nitroglycerin. P. DEEG and K. W. SCHNEIDER	214
Discussion	221

Part V Vascular Effects

Comparative Vasodilating Effects of Nitroglycerin and Verapamil on Large Coronary Arteries in Man. A. L'ABBATE, O. PARODI, I. SIMONETTI, MARIA GIOVANNA TRIVELLA, M. BARONI, and G. VALLI	224
Quantitative Coronary Angiography: Effect of Isosorbide Dinitrate on Coronary Artery Stenoses. W. RAFFLENBEUL, F. URTHALER, R. O. RUSSELL, T. N. JAMES, and P. R. LICHTLEN	231
Threshold Dosages of Nitroglycerin for Coronary Artery Dilatation, Afterload Reduction, and Venous Pooling in Conscious Dogs. E. BASSENGE, J. HOLTZ, H. KINADETER, and A. KOLIN	238
Influence of Nitroglycerin on Aortic Compliance, Capacity of the Windkessel, and Peripheral Resistance. G. SAUER, H.-H. WILLE, U. TEBBE, K.-L. NEUHAUS, and H. KREUZER	251
Echocardiographic Findings of Left Ventricular Function Before and After Isosorbide Dinitrate in Chronic Hemodialysis Patients. B. STEGARU, A. GEIGER, J. BUSS, O. VAN EYL, and M. STRAUCH	256
Hemorrhological and Hemodynamic Effects of ISDN in Essential Hypertension and Obliterative Arterial Disease. V. HOSSMANN, W. WEGENER, B. WEGENER, F. SABOROWSKI, and K. CÄSAR	263

Coronary Artery Spasm Combined with Walk-through Phenomenon – a Special Type of Prinzmetal's Angina. P. STÜRZENHOFECKER, L. GÖRNANDT, and H. ROSKAMM	271
Discussion	277

Part VI Pulmonary Circulation

Effect of Nitroglycerin on the Diameter of Peripheral Arterial and Venous Pulmonary Vessels. G. KOBER, R. GROSSMANN, W. SCHULZ, and M. KALTENBACH.	280
Nitrates in Patients with Pulmonary Hypertension Due to Airways Obstruction. H. MATTHYS, K. H. RÜHLE, and T. HALLER.	285
Comparison of the Effects of Nitroglycerin and Aminophylline on Hemodynamics and Lung Function in Patients with Chronic Obstructive Lung Disease. B. NIEHUES, W. JANSEN, H. OBERHOFFER, R. THOMA, H. J. KÜPPER, and D. W. BEHRENBECCK	293
Influence of Nitroglycerin on Central Hemodynamics and $\dot{V}_A/\dot{Q}_C$ of the Lungs in the Postoperative Period After Coronary Bypass Surgery. A. HOLMGREN, E. ANJOU, L. BROMAN, and S. LUNDBERG	299
Effect of Sustained-Release Isosorbide Dinitrate on Pulmonary Arterial Hypertension in Patients with Chronic Cor Pulmonale. M. PANTZER	310
Influence of Isosorbide Dinitrate of Pulmonary Circulation and Gas Exchange in Acute Respiratory Distress Syndrome. V. DRAXLER, W. MAURITZ, and P. SPORN	314
Discussion	322

Part VII Acute Myocardial Infarction and Unstable Angina

The Use of Sodium Nitroprusside in the Treatment of the Acute Phase of Myocardial Infarction. H. J. C. SWAN	324
The Role of Nitroglycerin in Acute Myocardial Infarction. W.-D. BUSSMANN	329
Nitroprusside and Nitroglycerin in Acute Myocardial Infarction. V. KÖTTER, T. LINDERER, and R. SCHRÖDER	341
The Effect of Intracoronary Nitroglycerin in Acute Myocardial Infarction. P. RENTROP, H. BLANKE, H. KÖSTERING, and K. R. KARSCH.	348
Panel-Discussion.	352
Intracoronary Thrombolysis in Evolving Myocardial Infarction. W. GANZ, N. BUCHBINDER, H. MARCUS, A. MONDKAR, L. O'CONNOR, J. MADDAHI, D. BERMAN, Y. CHARUZI, C. BEEDER, T. PETER, P. K. SHAH, W. SHELL, and H. J. C. SWAN	355

Feasibility of Nitroprusside Therapy in Patients with Hypotension Due to Severe Left Ventricular Failure in Acute Myocardial Infarction. W. MERX, R. V. ESSEN, R. ERBEL, J. MEYER, and S. EFFERT	359
Vasodilator-Induced Changes in Global and Regional Ventricular Function in Acute Myocardial Infarction. P. K. SHAH, M. PICHLER, F. SHELLOCK, D. BERMAN, and H. J. C. SWAN	362
A Randomized Trial of Prolonged Nitroglycerin Infusion in Acute Myocardial Infarction. P. CHICHE, S. BALIGADOO, and J. P. DERRIDA	363
Intravenous Nitroglycerin in Unstable Angina. A. PAGE, P. GATEAU, J. OHAYON, J. COUPILLAUD, D. LEMINH, and P. BESSE	371
The Action of Nitroglycerin on Pacing-Induced Arrhythmias. P. PROBST, C. SCHWARZER, and O. PACHINGER	377
Discussion	384

Part VIII Exercise

Assessment of the Effect of Isosorbide Dinitrate on Left Ventricular Hemodynamics at Rest and Under Exercise in Patients with CHD by Gated Blood Pool Scintigraphy. H. SIMON, M. BÄHRE, U. SCHUPPAN, H. P. BREUEL, R. KNOPP, C. WINKLER, and A. SCHAEDE	388
Influence of Isosorbide Dinitrate and Mononitrate on the Ejection Fraction and Wall Motion Parameters at Rest and Under Exercise in Patients with Coronary Heart Disease. M. STAUCH, P. KRESS, H. GEFERS, W. NECHWATAL, F. BITTER, H. SIGEL, and W. E. ADAM	396
Influence of Nitroglycerine on Myocardial Metabolism of Cyclic AMP, Cyclic GMP, Lactate, Free Fatty Acids, and Glucose at Rest and During Exercise in Patients with Coronary Heart Disease. V. HOMBACH, W. C. JANSEN, D. W. BEHRENBECK, M. TAUCHERT, B. NIEHUES, and H. HILGER	401
Attenuation of Nitrate Preload Reduction by Exercise in Patients with Severe Chronic Heart Failure. S. A. RUBIN, H. J. GELBERG, and H. J. C. SWAN	406
Sustained Effect of Isosorbide Dinitrate Ointment on Angina and Exercise-Induced Electrocardiographic Changes in Patients with Ischemic Heart Disease. D. BRUNNER, J. WEISBORD, G. NISSENMAN, and J. KLINGER	411
Exercise-Induced Nonischemic Angina Pectoris Due to Abnormal Left Ventricular Compliance: Effects of Nitroglycerin. H. OHLMEIER, U. GLEICHMANN, G. TRIEB, and H. MANNEBACH	419
Long-Term Effects of Isosorbide Dinitrate and Molsidomine on Left Ventricular Wall Motion and Dimensions in Patients with Coronary Heart Disease and Stable Angina Pectoris. H. W. HEISS, M. KÜNKEL, J. STAIGER, and H. JUST	424

Myocardial Oxygen Consumption and Coronary Blood Flow at Rest and During Exercise After Application of Nitroglycerin. W. C. JANSEN, V. HOMBACH, B. NIEHUES, M. TAUCHERT, D. W. BEHRENBECK, and H. H. HILGER	427
Effect of Isosorbide Dinitrate and Coronary Bypass Surgery on the Perfusion Distribution and Regional Tracer Uptake in 201 Thallium Stress Scintigraphy. R. WOLF, P. PRETSCHNER, H.-J. ENGEL, H. HUNDESHAGEN, and P. R. LICHTLEN	436
Effects of Nitrates at Rest and During Bicycle Exercise and Cross-Country Walking. H. WEBER, G. BERGHÖFER, W. RUTSCH, and H. SCHMUTZLER	445
Discussion	451

Part IX Chronic Heart Failure

Peripheral Circulation in Congestive Heart Failure. W. W. PARMLEY	454
General Principles of Treatment with Vasodilators. J. N. COHN	461
Chronic Refractory Pump Failure: Effects on Hemodynamics and Circulating Catecholamines of Intravenous Isosorbide Dinitrate. B. RABINOWITZ, I. TAMARI, E. ELEZAR, and H. N. NEUFELD	469
Treatment of Low-Output Failure After Open Heart Surgery with Nitroglycerin and Dobutamine. K. VAN ACKERN, N. FRANKE, K. PETER, and P. SCHMUCKER	473
Afterload Reduction with Dipyridamole and Preload Reduction with ISDN in Congestive Heart Failure. U. SIGWART, M. GRIBIC, G. TURINI, and J. L. RIVIER	479
Panel-Discussion	486
Effect of Nitroglycerin on Hemodynamics and Catecholamines in Patients with Left Heart Failure. W. W. KLEIN, R. GOEBEL, D. BRANDT, and E. MAURER	488
Dose Response Study of Acute Hemodynamic Effects of Intravenous Isosorbide Dinitrate in Patients with and without Heart Failure. S. BALIGADOO, J. C. INGRAND, CH. H. SAVIER, J. P. DERRIDA, and P. CHICHE	495
Comparative Efficacy of Nitroprusside and Prazosin on Cardiocirculatory Function in Chronic Congestive Heart Failure. N. A. AWAN, K. E. NEEDHAM, M. K. EVENSON, and D. T. MASON	505
Efficacy of Long-Term Nitrate Treatment in Chronic Left Ventricular Failure. J. A. FRANCIOSA and J. N. COHN	510
Haemodynamic Effects of High Dose Isosorbide Dinitrate (160 mg Daily) in Severe Congestive Heart Failure. K.-W. WESTERMANN, B. BENDER, G. FRICK, R. HÖGE, W. MÜLLER, and H. POKAR	516
Renal Changes in Low Cardiac Output Failure: Improvement with Vasodilators. J. A. MANTLE, R. O. RUSSELL Jr., W. N. TAUXE, H. D. DUSTAN, W. J. ROGERS, and C. E. RACKLEY	521
Discussion	528