SHOCK

PATHOLOGY
METABOLISM
SHOCK CELL
TREATMENT

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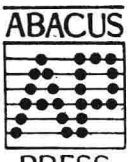

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This book was originally published in Romania in 1973 under the title Şocul, *with a Foreword by Mr Theodore Burghele, the President of the Academy of the Socialist Republic of Romania. The authors have been working as a team, under the guidance of the Professor of Surgery of the Bucharest University School of Medicine, Iuliu Şuteu, for a number of years and this volume is a summary of their discoveries and the conclusions they have reached on the intricate problem of shock states. For the English edition, the original text has been completely revised and up-dated and additional illustrations have been provided.*

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PREFACE

Shock has been recognized as a clinical syndrome for almost 2000 years, but today it is still a controversial phenomenon in the medical world. In the historical and geographical universe man is an infinitesimal entity subject to the action of a complexity of endo- and exogenous factors — the 'environmental pressure'. Contemporary life contains a great variety of harmful factors, of varied physical, chemical and/or biological origin that are the potential generators of *critical* situations, of true *states of shock*, from the viewpoint of medical pathology.

Conditioned by the outstanding technical progress in all fields, these deleterious factors increase in numbers and intensity at an unprecedented rate; their action, however, may be avoided, limited, prevented or removed. Although vast programmes of prevention have been drawn up, the world statistics communicated at the first International Symposium on accidents causing shock, held in Washington in 1970, gave impressive figures referring to trauma. Today it is known that one of ten inhabitants of the earth suffers yearly an injury that will necessitate several days hospitalisation, that two-thirds of the cases are youths, and that the care of a casualty with multiple injuries — in shock — demands a surgical intervention that often exceeds the complexity of cardiac surgery and transplant surgery; nevertheless, the organisation of centres of investigation and treatment of cases of severe trauma and shock is only in its initial stage in many countries. Among the present ecologic accidents is the 'trauma epidemic' which, unfortunately, occupies an important place.

Resulting from the multiple conflicts between human beings and the harmful factors of their environment, the world morbidity rate for trauma is greater than the morbidity rate for cardiovascular diseases, and four times that for cancer.

Apart from patients suffering from severe shock with acute functional imbalance, many are brought to operation or to intensive care units suffering from chronic diseases which result in severe functional and morphologic disturbances, and which justify the present notion of 'chronic shock'.

As a rule, in the clinic, a diagnosis of shock seems to be comparatively simple: cold or moist skin, arterial blood pressure below 80 mmHg, cardiac

index less than 2500 ml/min/m², urinary output less than 25 ml/hour and arterial standard bicarbonate below 2 mEq. But these criteria may become rigid and, therefore, useless if not followed up functionally. In point of fact, understanding of the complex phenomenology of shock implies a deep-rooted knowledge of the pathophysiology of shock and its fluctuating course.

When shock was conceived as exclusively haemodynamic, systemic arterial pressure served as a guide for the clinical stages and the therapeutic approach; later, when shock was understood at rheologic level, the criteria for assessing the stage of shock became the lowering of the effective circulating blood volume and perfusion of the microcirculation. The notion of 'shock viscus' was coined (shock liver, kidney, intestine, lung, etc.). In 1935, Alexis Carrel stated that 'Man is the hardiest of all animals, . . . however, our organs are fragile. They are damaged by the slightest shock. They disintegrate as soon as blood circulation stops'.

The next stage in our understanding of the phenomenology of shock 'descended' to the intimacy of the cellular enzymatic chains; for a long time lactic acidosis came to be considered the most reliable prognostic marker of the severity of shock.

Today we have gone beyond this stage. The pathobiochemical and pathobiophysical events in the course of shock are analysed at molecular and atomic level, where the very logic of the cybernetic and thermodynamic organization of the human body is actually disturbed. Therefore, considering the cell as the lesional site where the main endogenous antishock struggle takes place in the macrosystem, in writing this book we considered that the notion of *shock cell* offers the best basis for studying the disturbances produced by shock down to molecular level, particularly as Science in the last decade has furnished an avalanche of data useful for our understanding of the biologic occurrences. The thermodynamic approach to shock was possible by separate consideration and then integration in the behaviour of the energy subsystems in the shock cell. The characteristics of the shock cell also allow for systematization of the governing and control relationships between the cellular space and the extracellular space.

Most of the studies of the last few years deal with the cellular metabolic response to shock, and monitoring of the biochemical parameters most reliable for assessing the severity of shock. Monitoring has resulted in determination of flow parameters whose variations permit the institution of a prompt replacement of the fluid lost. It has become obvious that the hydroelectrolytic reaction to shock does not consist only in a simple loss of intravascular effective circulating fluid; studies have likewise been carried out on the role of the interstitium and lymphatics in shock, on crystalloids that are now being substituted for colloids for making up volume losses, especially in the first phases of shock. The first adverse responses to dextrans, mannitol, diuretics, etc. are recorded, and the much discussed electrolytic solutions have finally proved extremely useful, permitting re-equilibration of the interstitial space and decrease in the number of perfusions and, therefore, of the untoward post-transfusional reactions.

The reactions of the human body to shock are still imperfect and incomplete, a true shock-inducing agent always being a surprisingly intense pathogenic stimulus to which our homeostatic systems have not yet become fully adapted, and are not yet 'phylogenetically' aware. Therefore, the immediate endogenic measures the body takes, known at present as the *reactional syndrome*, are restricted by the inherent sacrifices this demands. Otherwise stated, the human body is at first panicstricken and tries to save itself by reacting over-hastily and, as a result, a certain disorder ensues which may sometimes in itself be fatal.

Prolonged selective vasoconstriction may give rise to irreparable damage in vital areas, among which the lung, today considered to be in man the most sensitive target organ of hypotension, hypovolaemia and septic states. On the other hand, enzymatic hyperglycolysis endeavours to supply energy to the shock cell, loading it, however, with protons up to the dangerous level of hydrolase autodigestion.

Almost all the occurrences with an immediate adaptive trend that appear in shock are of disproportionate intensity and duration, impeding the therapy that has at times to attenuate or stimulate these same occurrences, depending on the state of shock.

The alpha effect of catecholamines is at first useful both haemodynamically and metabolically (proven by selective blocking with bretilium tossilate of norepinephrine release which has never improved but, on the contrary, aggravated shock), but an excess of alpha stimulation is harmful if it persists in certain areas. Thus, α-lytic drugs have gained favour in the therapy of shock but they do not yet occupy an important place because excessive dilatation of the microcirculation, which they bring about, may be dangerous and difficult to control.

In order to emphasize the uncertainty of the therapeutical measures taken today it is sufficient to recall that some authors recommend β-stimulating drugs (especially in cardiogenic and bacteraemic shock) and others use β-blocking agents (especially for the pulmonary protection they offer). The favourable action of catecholamine precursors in the late phases of shock is likewise well known, while α-stimulants are administered with great care in bacteraemic shock because of their antiphlogistic effect.

Although of bewildering aetiologies, the numerous types of shock encountered in the clinic have a common pathophysiological centre whose segments fall into a fundamental and characteristic biological pattern.

It is almost unanimously recognized today that shock has a multiphase, oscillating development, but the moment of transition from one phase to another is difficult to establish clinically. These phases are, however, of great practical importance since they at times impose paradoxical changes in the treatment applied which must follow closely in the wake of the progressive waves of shock and exercise a continuous intracellular action sustaining the enzymatic and membraneous apparatus.

The oscillating course of shock is also unpredictable, differing entirely from the usual systemic reaction of the after-effects of an injury; hence,

in its dynamics, shock often reaches the borderline of irreversibility over which it will pass in the absence of adequate treatment.

It is not yet known for certain, especially at clinical level, which are the limits of the reversible-irreversible; it appears certain, however, that this point is decided at the level of the *shock cell*, long before the terminal clinical signs appear. In the intimacy of cellular metabolism certain transformations occur a long while before they become clinically apparent; therefore the clinician must be permanently aware of the state of shock at enzymatic level and that of the functional reflexes of nucleic acids, so that the intracellular introduction of each therapeutical gesture must be borne in mind. The clinic thus acquires a deeper perspective, without losing its fascinating facet, an insight into the intracellular source of life, the old term of 'clinical picture' taking on three dimensions and becoming a 'clinical relief'.

The surgeon of today is almost always aware of the pathophysiological axis of shock, and faces, together with the anaesthetist-resuscitator, problems of tissular hypoperfusion and disturbances in the homeostasis of the human body at every step.

'The modern surgeon must be acquainted with surgical pathophysiology', asserts Prof. Th. Burghele, recalling at the same time the classical condition announced by René Leriche: '. . . for the sake of quality the surgeon of today must rise from the rank of anatomist to the dignity of physiologist'.

The chapters deal with different aspects in the study of shock and may therefore seem to be unbalanced. The themes contained in previous well-known works may only be outlined or merely mentioned in some chapters, or dealt with in detail in others and then taken up again in further chapters where the subject of shock was deemed to be insufficiently treated or needing to be brought up to date.

The reader will not find in this book precise instructions but only principles concerning the investigation and therapy of each type of shock. The great variety of clinical aspects calls for individual consideration of each particular case; hence we have avoided any attempt at a schematical representation.

This is not a book on clinical practice and treatment of shock but a discussion on the pathophysiology of shock, based on the biological perspective of this phenomenon and with additional new data on biochemical, hormonal, genetic, cybernetic, rheodynamic and thermodynamic aspects with an attempt at bringing into relief some of the facets that until recently have been neglected.

To those who will perhaps regret that certain facts or ideas have not been sufficiently emphasized we answer by quoting Montesquieu: 'When treating a subject it is not necessary to exhaust it; it is sometimes sufficient to draw attention to it'.

Long-term investigation of a complex biological phenomenon such as shock calls for team work and presupposes the cooperation of numerous

specialists. The authors of this volume undertook the role of initiating the experimental models and of promoting their implementation; they also made the decision to combine experimental findings with clinical experience and, especially, to take on the responsibility of gathering together suitable material about shock, which by its very nature is composed of diverse elements.

The studies were carried out in Bucharest in the Department of Experimental Medicine of the Central Military Hospital (Dr T. Giurgiu) and the Department of Experimental Nuclear Medicine of the Fundeni Clinical Hospital (Dr O. Cavulea). Histologic examinations were performed and interpreted in the Laboratory of Pathologic Morphology of the Central Military Hospital (Dr I. Strîmbeanu). The biochemical constants and plasma enzymes were determined in the Laboratory of Biochemistry of the same hospital (pharmacist Dr C. Apreotesei) and haematologic studies in the Center of Haematology of the Armed Forces (Dr C. Iercan and Dr R. Perlea) and the Laboratory of Haematology of the Central Military Hospital (Dr C. Satmari).

We wish to express our gratitude to all who have participated and contributed so generously in the multiple themes required in the study of shock; we likewise acknowledge our grateful thanks to doctors D. Singer, P. Ionescu, D. Bărboi, T. Safta, A. Verdeş and a numerous group of enthusiasts without whose practical aid and advice our endeavours would have been inadequate.

To our colleagues who by their work and skill down the years have made of our team a closely knit working unit, we owe more than a debt, for this volume belongs to them, too, to an equal extent.

Our most cordial thanks are due to Prof. Ion Teodorescu-Exarcu for his outstanding help, comments and advice.

We cannot say how deeply indebted we are and how much we value the work of our colleagues in the field of medicine, whatever their specialty, who meet at the patients bedsides to allay their daily suffering by understanding, self-denial and professional integrity.

The editors of the Military Publishing House have always been solicitous and have constantly shown a keen interest in medical publications; thanks to them transforming a rough manuscript into a published book became a pleasant work of collaboration.

THE AUTHORS

Bucharest, December, 1976.

ABBREVIATIONS

AB	actual bicarbonate
ACTH	adrenocorticotrophic hormone
ADH	antidiuretic hormone
ADP	adenosine diphosphoric acid
AMP	adenosine monophosphoric acid
ARAS	ascending reticular activating system
ARF	acute renal failure
ATP	adenosine triphosphoric acid
ATP-ase	adenosine triphosphatase
AV shunt	arteriolo-venular shunt
BB	buffer bases
BE	base excess
BP	blood pressure
CI	cardiac index
cAMP	cyclic AMP (3', 5', AMP)
Cit a, b, c, etc.	cytochrome a, b, c, etc.
CITOX	cytochrome-oxidase
CNS	central nervous system
CO	cardiac output
CoA	coenzyme A
$CO_{2\ total}$	total carbon dioxide
COMT	catechol-ortho-methyl-transferase
CRF	corticotrophic releasing factor (*see* CRH)
CRH	corticotrophic releasing hormone
C_2SC_0A	active acetate
CSF	cerebrospinal fluid
CVP	central venous pressure
DHAP	dihydroxyacetone phosphate
DIC	disseminated intravascular coagulation
DNA	deoxyribonucleic acid
DOCA	deoxy-11-corticosterone acetate
1,3-DPG	1,3-diphosphoglycerate
1,2-DPG	1,2-diphosphoglycerate
ECBV	effective circulating blood volume
ECG	electrocardiogram
EM	Embden-Meyerhof cycle
EMK	Embden-Meyerhof-Krebs cycle
FA	acid phosphorylase
FAC	acid phosphatase
FAD	flavinadeninedinucleotide
FFA	free fatty acids
FFAC	free fatty acids cycle (Lynen)
FSH	follicular stimulating hormone
FSRH	follicular stimulating releasing hormone
FT	total phosphorylase
FWC	free water clearance
F-6-P	fructose-6-phosphate
F-1,6-DP (FDP)	fructose-1,6-diphosphate
GABA	gamma amino-butyric acid
GFR	glomerular filtration rate
GH (*see* STH)	growth hormone
GOT	glutamic oxalacetic transaminase
GPT	glutamic pyruvic transaminase
GRH	growth releasing hormone
GSH	hydrogenated glutathione

GSSG	dehydrogenated glutathione
G-1-P	glucose-1-phosphate (Cori ester)
G-6-P	glucose-6-phosphate (Robison ester)
G-6-Pase (G-6-PA)	glucose-6-phosphatase
G-6-PDH	glucose-6-phosphate-dehydrogenase
Hb	haemoglobin
HbO_2	oxyhaemoglobin
HES	hydroxyethyl starch
Ht	haematocrite
ICP	intracranial pressure
IDH	isocitric-dehydrogenase
IgM (IgG, IgE, etc.)	immunoglobulin M, G, E, etc.
ICSH	islet cell stimulating hormone
K_i	intracellular potassium
K_e	extracellular potassium
LDH	lactic-dehydrogenase
LH	luteinizing hormone
LPEP	leucinaminopeptidase
LRH	luteinizing releasing hormone
LTH	luteotrophic hormone
MAO	monoamino-oxidase
MDF	myocardial depressor factor
MDH	malic-dehydrogenase
NAD	nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotide phosphate
Na_i	intracellular sodium
Na_e	extracellular sodium
OAA	oxaloacetic acid
OP	oxidative phosphorylation
OPC	oxidative phosphorylation chain
PAOR	postaggressive oscillating reaction
PASR	postaggressive systemic reaction
PIOR	postinjury oscillating reaction
PISS	postinjury systemic syndrome
PEP	phosphoenolpyruvate
PFK	phosphofructokinase
PGDH	phosphoglyceraldehyde-dehydrogenase
PVP	polyvinyl pyrrolidon
PCO_2	partial carbon dioxide pressure
P_aCO_2	partial (arterial) carbon-dioxide pressure
P_aO_2	partial (arterial) oxygen pressure
P_vO_2	partial (venous) oxygen pressure
P_vCO_2	partial (venous) carbon di-oxide pressure
P_AO_2	partial (alveolar) oxygen pressure
P_ACO_2	partial (alveolar) carbon dioxide pressure
pH_a	actual *p*H
RBC	red blood cell
RBF	renal blood flow
RES	reticuloendothelial system
RF(RH)	releasing factor (releasing hormone)
RI	respiratory index
RNA	ribonucleic acid
SB	standard bicarbonate
SDH	succinic-dehydrogenase
SFEZA	sulphatase
STH *(see* GH)	somatotrophic hormone
T_3	triiodothyronine
T_4	thyroxine
THAM (TRIS)	trihydroxymethylamino-methane
TPR	total peripheral resistance
TRF	thyrotropic releasing factor
TRH	thyrotropic releasing hormone
TSH	thyrostimulating hormone
UO	urinary output
VDM	vasodilatator material
VEM	vasoexcitator material

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