Burns, shock, and plasma volume regulation

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With 138 illustrations

The C. V. Mosby Company

Saint Louis 1967

Printed in the United States of America

Library of Congress Catalog Card Number 67-26087

Distributed in Great Britain by Henry Kimpton, London

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To our wives

Alice Moyer and Marilyn Butcher

Self-denying and devoted

Preface

This book has been written to present the authors' concept of the treatment of shock and burns. Because of the lack of adequate experimental data in many areas, there is still much uncertainty about the best way to conduct the therapy of a particular patient suffering from thermal injury or from peripheral circulatory failure, whatever its cause may be. We hope that if this book accomplishes nothing else, it will at least serve to heighten the physician's sense of therapeutic ignorance and ministrational inadequacy in the areas of shock and burns.

The therapy of shock and burns is still far short of perfection, largely because the practice of medicine is an art. It is an art because it is a way of doing, just as is navigation. And just as navigation is an art, having the scientific bases of astronomy, chronography, and electronics, so medical therapeutics is an art based on such sciences as anatomy, pathology, chemistry, physics, psychology, microbiology, and system and cellular physiology. In view of today's paucity of knowledge in many areas within the purview of these physical and biologic sciences, medical therapeutic art can only be highly imperfect at best. Another factor that has kept medical therapeutic art from advancing as rapidly as it might is empiricism. The therapy of shock and thermal injury is still stultified by it, and it must be so until our knowledge of cellular and system biology is far more perfect than it is today. Until the biologic sciences, to which the art of the therapy of shock and burns is principally related, are better developed, improvement in therapy of shock and burns must come mainly from critical experimental and clinical evaluations of extant empirically based therapeutic practices employing rigorously applied bioassay techniques with recovery and death as the criteria of efficacy. Bioassay methods applicable to the study of therapeutic efficacy are illustrated and used in this text.

C. A. M.
H. R. B.

Acknowledgments

We wish to extend special thanks to the following individuals who contributed so much in the completion of the manuscript for this book:

Margaret Biasi, for expert and meticulous editorial work without which the book would not have been written.

Kathleen Marsh, Administrative Secretary of the Department of Surgery, Washington University School of Medicine, who so lightened our administrative loads that we had time for personal participation in the laboratory and clinical investigative work.

Patrick G. Graham, M.D., who so skillfully and steadfastly attended the first cases of very extensive burns treated with the continuously wet silver nitrated dressing.

George L. Tucker, M.D., and Patricia Maxwell, R.N., who worked indefatigably on the problems encountered during the unsuccessful attempt to treat very extensive burns with the continuous saline bath. It was this experience that led to the abandonment of the saline immersion treatment and provided the impetus for the development of the silver nitrated dressing technique. Miss Maxwell later contributed greatly to nursing in the Hartford Burn Unit.

Margaret Linss, R.N., for her devoted attendance to the burn patients and for expert administration of the Hartford Burn Unit.

Daniel L. Gravens, who performed the bacteriologic work involved in the in vitro and in vivo testing that led to the clinical use and evaluation of 0.5% silver nitrate as a bacteriostatic agent.

Harry W. Margraf, for his expert and timely development and meticulous performance of the microchemical blood analyses that constituted important bases of all of the laboratory and clinical investigations performed in the Flora and Harry Freund Surgical Research Laboratory and the Barnes Hospital.

William W. Monafo, M.D., who expertly and diligently assisted in the supervision of the work of house officers and the care of the ill in the Hartford Burn Unit and personally contributed much to the bacteriologic investigations.

We should also like to extend our thanks to the following organizations,

without whose assistance, financial and otherwise, investigations into the problems and treatment of burns would not have been possible.

Washington University School of Medicine, Saint Louis, Missouri
Harry Freund Memorial Foundation, Saint Louis, Missouri
John A. Hartford Foundation, Inc., New York City
Flora and Harry Freund Surgical Research Laboratory, Saint Louis, Missouri
United States Public Health Service

The following house officers, nurses, and medical students contributed materially to laboratory or clinical investigations.

Khurshed A. Ansari, M.D.
Loreno Brentano, M.D.
Peter W. Broido, M.D.
William A. Burke, M.D.
Dale F. Burton, M.D.
Fred T. Caldwell, Jr., M.D.
John S. Dillon, M.D.
R. H. Fallon, M.D.
Frederick J. Finseth, M.D.
Walter B. Goldfarb, M.D.
Molly Granger, R.N.
Ted L. Grayson, M.D.
Robert A. Grummon, M.D.
Michael E. Holzer, M.D.
Martin B. Harthcock, M.D.
Richard Kempson, M.D.
Vivian Kempson, R.N.
Judith Kinder, R.N.
Lawrence J. Lynch, Jr., M.D.
Patricia McDonnough, R.N.
Sandra Mitchell, R.N.
John A. Moncrief, Lt. Col. U.S.M.C.
Bryce L. Munger, M.D.
Richard Meyers, M.D.
David Nelson, M.D.
Shemuel Nissan, M.D.
Howard L. Nudelman, M.D.
H. D. Onken, M.D.
J. L. Osterholm, M.D.
Hiram C. Polk, Jr., M.D.
Basil A. Pruitt, Jr., Capt. U.S.M.C.
Judith Rashet, R.N.
Stephen J. Shochat, M.D.
Richard C. Shaw, M.D.
N. D. Sower, M.D.
Ronald Ullman, M.D.
Dennis Venzon, M.D.
Jacob E. White, M.D.

Contents

Part I

Blood volume regulation

Chapter 1

An understanding of the factors influencing blood volume regulation*

A direct qualitative relationship between plasma volume and corporeal sodium mass was first discovered in 1935 by Darrow and Yannet.[10] This was amply confirmed in 1951 by Cizek, Semple, Huang, and Gregersen,[7] who also found that plasma volume fell as sodium salts were removed from the body—even though no change in total body water occurred—unequivocally showing plasma volume to be a function of the amount of sodium salts in the body. However, the role of sodium salts in maintaining plasma volume appeared to be minor in that attempts to restore blood volume with saline after hemorrhage in man were seemingly ineffective.

Following extensive and careful bleeding experiments on unanesthetized man, Ebert, Stead, and Gibson[13] reported in 1941 as follows:

> The slow increase in plasma volume [*after hemorrhage*] is not the result of the lack of fluid in the body with which to dilute the blood, because when a physiologic solution of sodium chloride is given intravenously the dilution is not maintained. In these experiments it appears that after the initial period of dilution the size of the plasma volume is determined by the quantity of circulating protein. Therefore, a large increase in plasma volume is not maintained until the amount of circulating protein has been increased.
>
> It is established that in cases of surgical shock and of profuse hemorrhage with marked fall in blood pressure physiologic solution of sodium chloride is ineffective in treatment and that only the administration of whole blood or of plasma will produce a lasting rise in blood pressure. Apparently the diminished blood volume can be increased to only a limited degree by the addition of protein-free fluid. Beyond this point it is necessary to add a substance which increases the colloid osmotic pressure of the blood in order to increase the blood volume further.†

The second paragraph of the above quotation expresses the extant belief held by physiologists and clinicians alike.

*This work was supported in part by U. S. Public Health Service grants HE-02569 and HE-10389 and the U. S. Army.

†From Ebert, R. V., Stead, E. A., Jr., and Gibson, J. G., Jr.: Response of normal subjects to acute blood loss, with special reference to the mechanism of restoration of blood volume, Arch. Intern. Med. 68:578, 1941.

Nevertheless, others have found that saline solution is effective in treating hemorrhagic shock in animals. This was first critically demonstrated by Rosenthal and associates.[41] They found that 0.9% of sodium chloride was as effective as blood in treating hemorrhagic shock in mice, provided that the amount of saline solution administered was three times as great as the amount of blood that would effect recovery. They also found that serum was no more effective than saline solution in treating hemorrhagic shock.[36] These observations were amply confirmed by Sayers and associates.[37]

More recently (1959 to 1964),[22] during the investigation of the effects of enteral sodium depletion on chronically alcoholic and normal men and women and on anesthetized dogs depleted of sodium by peritoneal dialysis with 10% mannitol, the plasma volumes of the blood samples, as well as the measured circulating plasma volumes during sodium depletion, were found to be single-valued functions of the sodium load. The plasma volumes decreased $\cong$ 4.2% of the originals per milliequivalent of negative sodium load per kilogram of body weight[22] (pp. 5 and 6). During the depletion of sodium salts, the concentrations of plasma protein bore an arithmetic inverse relationship to sodium load—the concentrations rising 0.39 gm./100 ml. ($\cong$ 2.5 mm. Hg colloid osmotic pressure) per milliequivalent of sodium deficit per kilogram.

The projection of the curves of plasma volumes relative to negative sodium load to their intercepts with the X axis defined a point assumed to be the negative load of sodium, if obtainable, at which the plasma volume would be zero. This intercept of Y on the X axis occurs at a negative load of approximately 24 mEq./kg. (Acute negative sodium loads greater than 14 mEq./kg. are lethal for the dog; consequently, this assumption cannot be verified.) Because at this point all the sodium in the plasma (6 mEq./kg.) theoretically would be exhausted, 18 mEq./kg.

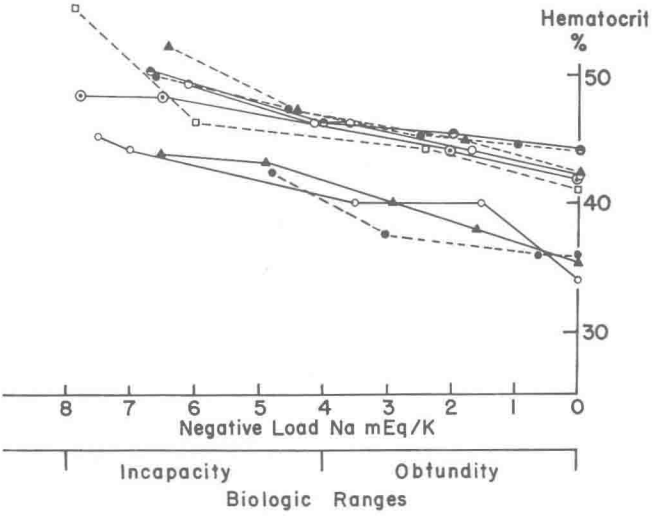

Fig. 1-1. Change in hematocrit of 10 human beings (7 men, 3 women) during enteral sodium depletions. (From Grayson and others: Ann. Surg. **158**:840, 1963.)

would need to come from extravascular sources—a ratio of 3 mEq. extravascular to 1 mEq. intravascular. This was the actual ratio of the contributions to the total deficit of sodium coming from the extravascular and intravascular compartments during the sodium depletions in man and dog.

Changes in the hematocrit while the hemoglobin concentration in red cells remained constant and sodium was depleted enterally from human beings for a period of 2.5 to 4 days are shown in Fig. 1-1. The hematocrit is plotted against negative load of sodium in milliequivalents of sodium per kilogram of body weight; the arithmetic linearity of relationship is readily visible.

Measurements of blood volume by three methods during progressive sodium depletion are shown in Fig. 1-2. After the initial ^{131}I measurement, the changes in hematocrit and in plasma protein concentration were also used as bases for calculating the change in plasma volume.

Changes in the plasma volume–plasma protein concentration and hematocrit of one individual during enteral Na^+ depletion are shown in Fig. 1-3. The concentrations of globulin and albumin, the plasma volume, and the hematocrit all changed linearly with the changing sodium load—the plasma volume *directly* and the protein and red blood cell concentrations *inversely*. The time of the experiment was 72 hours. The experiment was discontinued when the blood pressure fell to a dangerous level.

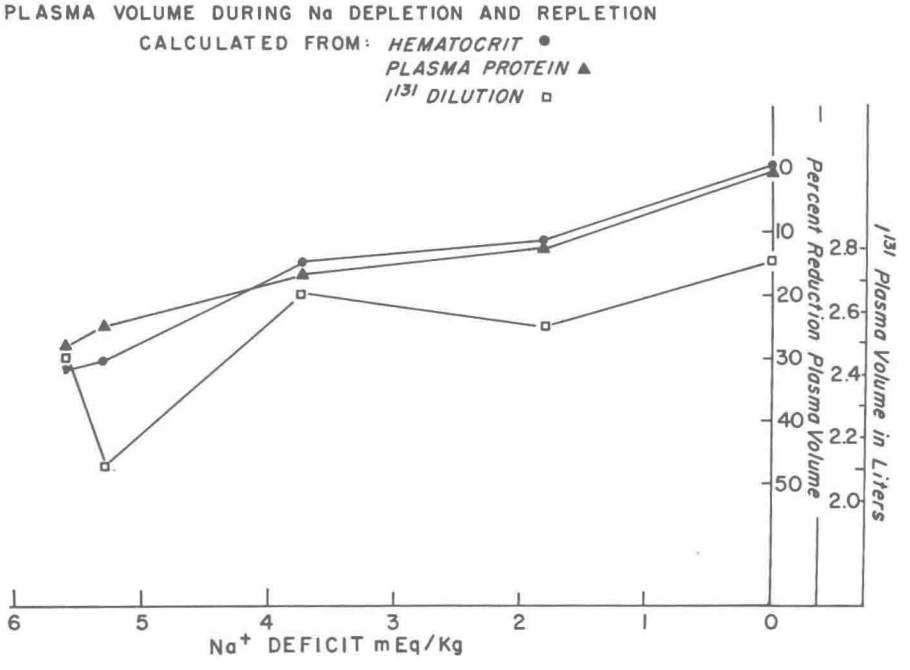

Fig. 1-2. Changes in plasma volume associated with sodium depletion in normal human being during 3½ days. Three bases of calculation were used. (From Moyer and others: Arch. Surg. **90**:799, 1965.)

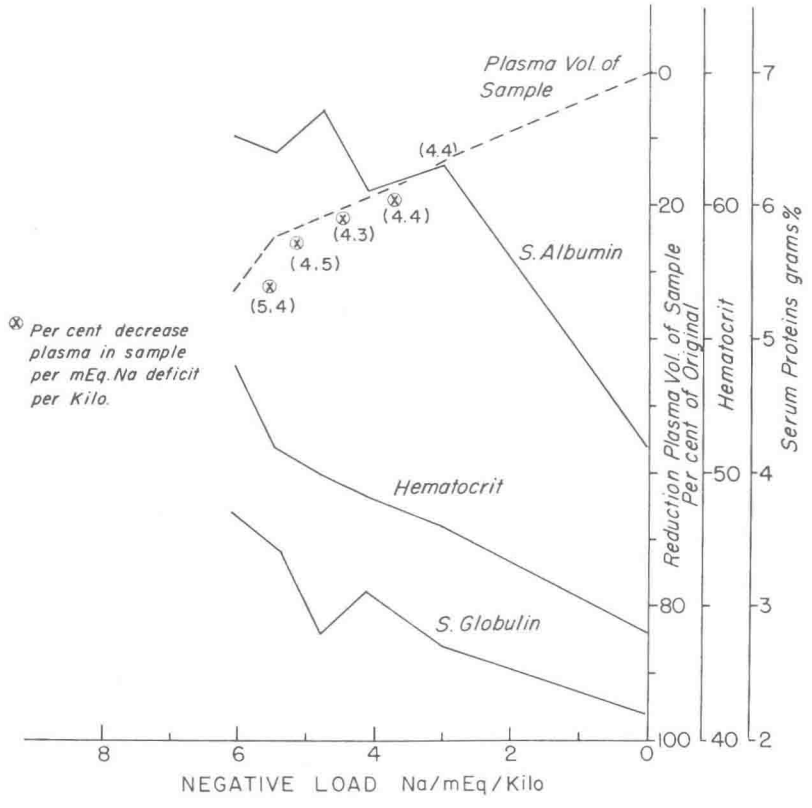

Fig. 1-3. Changes in plasma volume, hematocrit, and plasma protein concentrations associated with Na^+ depletion in a man. (From Grayson and others: Ann. Surg. **158**:840, 1963.)

Clearly within the range of sodium depletion compatible with adequate circulation in man, plasma volume is a single-valued function of the exchangeable sodium mass of the body. The colloid osmotic pressure, although it rises steadily during sodium depletion, exerts no detectable retarding influence upon the rate of reduction of plasma volume per unit of sodium deficit.

The discovery of the linear relationship of plasma volume to sodium deficit ($Y = {}^{-}.042\ X^*$) led to the question: If this is biologically true, then cannot hemorrhagic oligemia be immediately and permanently corrected with an appropriate isotonic sodium-containing solution devoid of colloid, notwithstanding all statements to the contrary? In an attempt to answer this question, the following experiments were performed:

1. The repletion of the blood volumes of splenectomized dogs 1 to 1½ hours after measured hemorrhages amounting to 20 to 45% of the original blood volumes

*Y = Plasma volume in percent of original.
X = Milliequivalents of sodium deficit per kilogram of body weight.

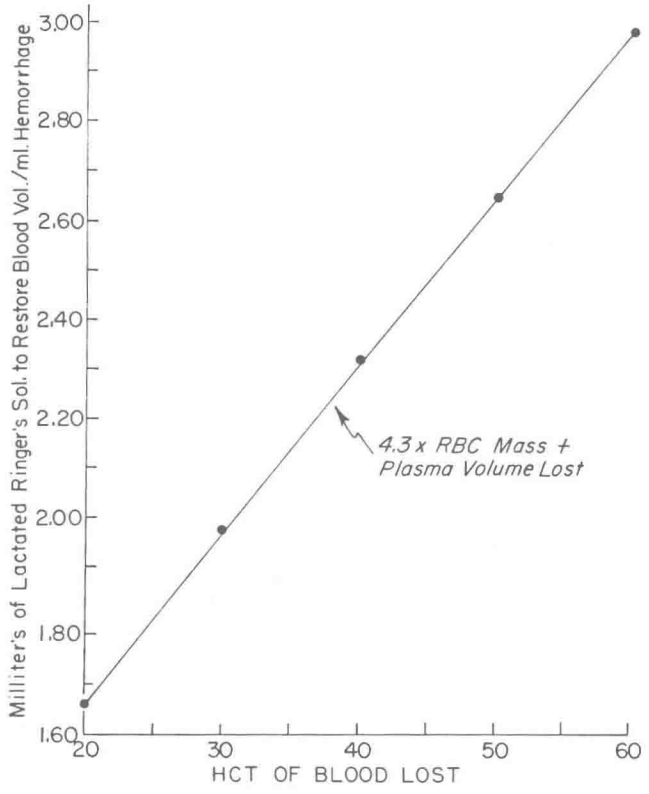

Fig. 1-4. Curve calculated from slope of decrease of plasma volume relative to sodium and water loads during enteral sodium and water depletions of human beings.

2. The immediate replenishment of acute bleedouts in normal and splenectomized dogs amounting to 52 to 70% of blood volumes
3. The repletion of blood volumes of normal men after measured venous bloodlettings amounting to 10 to 20% of the blood volumes
4. The comparative evaluation of the effectiveness of saline solution and autotransfusion in the treatment of oligemic shock in dogs

Methods

Lactated Ringer's solution (pH 7.6 to 8.2) was the saline solution used in all of the experiments. The volume of this solution given to each subject was calculated with the use of a graph (Fig. 1-4).

All the animals used were healthy, dewormed, and distemper-vaccinated adult dogs that had been quarantined for 3 weeks under the supervision of a veterinarian.

The general care of the dogs during all of the experiments consisted of light general anesthesia with sodium pentobarbital (30 mg./kg. intravenously), oral intratracheal intubation, and continuous monitoring of rectal temperature with

maintenance of body temperature at 37.6° C. ± 0.6°. The position of the unrestrained animal on the dog board was changed frequently to prevent atelectasis.

All blood returned into the animals was heparinized (3 mg. of sodium heparin per 1,000 ml. of blood) and handled in sterile glassware. Precautions were taken to prevent bacterial contamination of the wounds.

Upon completing the experimental observations, all cannulated arteries were ligated, and the groin wounds were closed with subcuticular sutures of catgut. The animals were closely attended until they recovered from anesthesia. When their temperatures had returned to normal they were then placed in cages in the general animal quarters.

Techniques of calculations used

1. Theoretical residual R.B.C. volume $= \left(\text{Initial RISA* blood volume} \times \frac{\text{HCT}}{100}\right) - \left(\text{Accumulative volume of blood removed} \times \frac{\text{HCT}}{100}\right)$

2. Residual blood volume calculated from HCT $= \dfrac{\text{Theoretical residual R.B.C. volume (ml.)} \times 100}{\text{HCT of blood expressed as whole number}}$

3. Plasma protein, method I

$$\text{Residual blood volume (ml.) calculated from plasma protein concentration} = \frac{\text{Residual circulating protein† (gm.)}}{\text{gm./ml. plasma protein in plasma}} + \text{Theoretical R.B.C. volume (mg.)}$$

4. Plasma protein, method II

$$\text{Residual blood volume (ml.) calculated from plasma protein concentration} = \frac{\text{Residual circulating protein† (gm.)}}{\text{gm./ml. plasma protein in plasma} \times (100-\text{HCT})}$$

A large difference between 3 and 4 signifies that protein has entered or left the bloodstream in significant quantity between the time of hemorrhage and the time the blood samples were drawn. When blood volume calculated by method I is larger than that calculated by method II, protein has *entered* the circulation, and when vice versa, protein has *left* the circulation.

EFFECT OF RINGER'S SOLUTION WITH LACTATE AND MACROMOLECULAR DEXTRAN IN SALINE UPON BLOOD VOLUME OF SPLENECTOMIZED DOGS

Saline replacement after acute hemorrhages of 20 to 45% of the blood volumes

Adult, healthy, nonpregnant female dogs (the spleen had been removed at least 2 weeks previously in some dogs) were lightly anesthetized with sodium pento-

*Radioactive iodinated serum albumin.

†Residual circulating protein = Centiliters of plasma volume × Plasma protein concentration (gm.%) − Centiliters of plasma removed × Plasma protein concentration of plasma removed (gm.%).