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FUTURE MEETINGS

Spring
April 13-18, 1980 — Anaheim, CA
April 12-17, 1981 — Atlanta, GA
April 18-23, 1982 — New Orleans, LA

Fall
October 15-19, 1979 — New Orleans, LA
October 12-17, 1980 — Toronto, Canada
November 1-6, 1981 — Boston, MA
October 10-15, 1982 — San Diego, CA

Specialty
Relation Between Neurotransmitters and Endocrine Functions
August 22-24, 1979 — East Lansing, MI

28th International Congress
July 13-19, 1980 — Budapest, Hungary
From Occidental College, where he was a football and track star, Dill received the B.S. in 1913 and later an honorary D.Sc.; from Stanford, the M.A. in 1914, and the Ph.D. in 1925. The years away from Stanford were spent teaching chemistry (1914-16), during which time he was married to Olive Lillian Cassel, a classmate at Occidental and a school teacher. Through the academic year 1916-17, Dill was principal of the El Dorado County High School in Placerville, California, where their daughter, Eliza beth Cassel, was born. Then for a year he was principal at the Palo Alto High School. This led to an appointment as a chemist with the USDA, wartime, Fisheries Research project. For this project, Dill served in a San Pedro laboratory. The Dill family at this time lived in south Los Angeles and here their son, David Bruce, Jr., was born. From San Pedro, Dill was transferred to San Diego and later, in 1921, to Seattle, where he was chemist in what is now the Food and Drug Administration.

The years 1923-25 were at Stanford and Dill received his Ph.D. with more help from his Uncle Lou, who had left him $1000 and a Dodge. The doctorate was in chemistry under Carl Alsborg, a director of the Food Research Institute. While a post-doctoral student at Strassburg, Alsberg had become a close friend of L. J. Henderson, a new Harvard M.D., and this led to Dill's obtaining an NRC fellowship in chemistry to work with Henderson. The setting developed to be the Massachusetts General Hospital rather than the Medical School, since Henderson had shifted positions from the Medical School to the University proper. At Harvard, Henderson also shifted Dill's interest to the physical chemistry of blood proteins. Through this, he established his long-lasting friendships and working relationships with A. V. Bock and J. H. Talbott and with many others; Fuller Albright, Chester Jones, Walter Bauer, Paul White, and Howard Means became good friends. During his two years at the Massachusetts General Hospital, he and Bock wrote a 3rd edition of Bainbridge's monograph, *Physiology of Muscular Exercise*, at the request of A. V. Hill. A secondary consequence of this effort was the initiation of studies on exercise physiology which has continued to this day. Exercise was considered as a stressing agent to be superimposed upon other stressors to more clearly identify the cardio respiratory capabilities and adjustments of the active organism.

Meanwhile, Henderson together with his friends, Dean Donham of the Business School and Dean Edsall of the Medical School, had conceived of the Harvard Fatigue Laboratory. (The history of the Fatigue Laboratory was published in 1973 by Prence-Hall, Inc.) They obtained two large Rockefeller grants, the Laboratory was given space at the Business School, and Dill was appointed to organize and direct the program of the Laboratory. As Dill says, "(The Laboratory) could well have been called the Laboratory of Environmental Physiology, for that is what it became." The academic appointment was as assistant professor in biochemistry at the School of Public Health, where he held a position from 1927-36. From 1927-47, he held professorships in industrial physiology at the Business School and was on Harvard faculties, in one capacity or another, until retirement in 1961 from a visiting lectureship in physiology at the School of Public Health. He continued to be director of research at the Fatigue Laboratory until 1947, although never with an official appointment for that responsibility.
The Fatigue Laboratory continued the work on the physical chemistry of the blood as commenced at the Massachusetts General by Henderson and Bock, at the same time maintaining close collaboration with Bock's laboratory. An indication of the quality of Dill's research can be found in the continued reference to and use of the oxygen dissociation curve described by him and his collaborators and which was published a half century ago (Fig. 1). The Fatigue Laboratory enlarged its interests and productivity to include exercise physiology, nutritional interactions, aging, and other stressors—high-altitude and climatic. Dill anticipated the need of the military for scientific support during World War II and with associates and friends served at the Aeromedical Laboratory and participated the need of the military for scientific support during World War II and with associates and friends served at the Aeromedical Laboratory research unit at Wright Field for the Army Air Forces (1941-43), then the Army Quartermaster Corps (1943-47); and, after that, as director of medical research, U.S. Army Chemical Research and Development Laboratory (1947-61).

Bruce Dill's decision to accept the position of medical research director at Edgewood must have come after a long and agonizing evaluation. It was quite apparent that he would be removing himself from the direct involvement with research and that in the future his role would be the "stimulator" and "facilitator" of research by others. He would function as an originator of research programs, a searcher for the best investigators to carry out and implement the basic idea, and provide the necessary financial and intellectual fostering to complete the research activity. Nonetheless, he performed this complex role until his retirement and delighted in the success of his investigators. A particular example of the latter was the support provided for A. S. Gordon to study, from a physiological viewpoint, better methods of artificial respiration. These investigations led to the present approach to cardio-pulmonary resuscitation-procedures which have saved so many lives. During those years, Dill's interest in exercise physiology, physico-chemical properties of blood, environmental physiology, and aging—areas in which he has received numerous awards, honors, and the respect of his fellow scientists and students—have continued to receive enthusiastic approbation. Dill opened new areas of research with his interests in the adaptability of the young and the aged to stressors. In fact, this adaptability principle has been examined in a couple of ways besides laboratory and field research forays, through the "News from Senior Physiologists" section of The Physiologist (instituted by Dill and conducted with others), and with the employment in the laboratory of high school students who are interested and may be stimulated to continue in science or medicine. One of Bruce Dill's proudest moments took place at the Physiological Society's fall meeting held at UC Davis. A 16-year old student of his presented a paper and conducted herself so well that she received enthusiastic approbation.

Dill has been a pioneer in several fields—exercise physiology, physico-chemical properties of blood, environmental physiology, and aging—areas in which he has received numerous awards, honors, and the respect of his fellow scientists and students. Now he is Research Professor at the Desert Biology Research Center, University of Nevada, Las Vegas.
Dear Dr. Reynolds:

"David Bohr's letter of 15 January 1979 inviting Retired Members to contribute to the coffers of the Society was an effective stimulus to make us think about the Society and its meaning to us, to more active physiologists, and the community.

"In spite of the current economic pressures, I believe that most of us Senior Physiologists are in a position to help our Society with an annual (at least) contribution.

"The fact that we have reached a certain age does not deny us the value of membership and most of the benefits, nor the opportunity to participate in Society activities and interests.

"Because Dave's letter mentioned the request to active members for a voluntary contribution of $10 - or more,' without underscoring the 'or more,' I venture a guess that most contributions have been $10.00. It would be unfortunate if that sum became 'fixed,' to help avoid that, I am sending you $25.00 for 1979, and hope to be able to continue to do so, so that APS can continue its many excellent services without the dues rising to a point where they become an obstacle to membership."

Sincerely,

(Name withheld by request)

P.S. I've just realized that this contribution is tax-deductible.

Dear Orr:

"I very much enjoyed the article which you published by Horace Davenport, 'A.N. Richards: or, Why I Don't Have An M.D.' I think that these rather personal historical pieces are apt to be very useful in the future. Obviously Horace has done a certain amount of digging through the literature although much of it comes from his own recollections.

"I was particularly interested that he knew about the controversy between Richards and Hirschfelder. I was a graduate student at the University of Minnesota in 1922, beginning in the fall actually. Consequently I was not there at the time Hirschfelder presented his April and May, 1922 papers to which Richards referred. However, there was talk about the fact that Richards was very unhappy about Hirschfelder's entrance into the field that he and Schmidt had been developing in 1921. However if Horace is right that Richards' published work on the subject with Wearn did not occur until 1924 and 1925, it would be a little peculiar that Richards would have simply said 'Professor Hirschfelder is apparently unaware of Wearn's report.' He would hardly have been aware of something reported in 1924 when he wrote in 1922.

"Horace goes on to say himself that 'there is something peculiar back of this.'

"I would have been interested in knowing what was really 'back of this' because Hirschfelder never admitted that he had been shown any work on PSP in Richards' laboratory. From other things that Horace says about the controversy I gather that he does not know either exactly why Richards was so upset.

"I myself have always had the highest respect for A.N. Richards and I am very pleased to see this good-humored personalized bit of biography.

"I suppose that I may be one of the relatively few people who was so pleased to see this appear in print. I hope I am wrong in this because I think that more of this type of writing would be good for our graduate students to read, if they do."

With best regards.

Sincerely,

Maurice B. Visscher

Dear Dr. Reynolds:

"I would like to take this opportunity to report that the expanded Associate Membership in APS has been extremely valuable to me.

"In my position here, I have limited time for research, but need to keep current on major developments in half of the interest areas within the whole scope of medical physiology. Many of the symposia in Federation Proceedings have been helpful beyond my expectations. I hope that this journal will remain available to Associate Members even if a further dues increase should become necessary."

Sincerely,

Thomas A. Lesh, Ph.D.
Associate Professor

The picture (above) and the following paragraph did not appear with Dr. Davenport's article because the photo was lost somewhere in the printing process. Dr. Davenport sent another copy and we now present the photo and the paragraph which related to it. "The last time I saw Richards was when I gave the third A. N. Richards Lecture to the Philadelphia Physiological Society. On the left is Phyllis Bott who did much of the micropuncture for Richards. In the middle is A. N. Richards with a martini in his hand. I will guarantee that he had two martinis and that he stayed awake during my lecture, which was pretty good for 85. The whiskey sour sticking out of the right side of the picture is in the hand of Grayson McCouch."
Recently I received a very impressive invitation from the Secretary of State to attend a briefing for the Scientific Community on the Second Strategic Arms Limitation Treaty.

The treaty with the Soviet Union is a stabilizing step toward reduction of delivery vehicles capable of intercontinental range and a concomitant, very real, reduction in the ability of each nation to destroy not only the other but probably the northern hemisphere. It will allow both parties to move away from the current, hair trigger, retaliatory weapons. Knowledge gained through the treaty mechanism will allow defensive planning on the basis of the USSR's real ability rather than on assuming the worst possible case. The Department of State envisions a continuum of SALT agreements, each being a small step.

Ambassador Marshall Schulman sketched current US-Soviet relations and stressed the need to build up their world esteem in areas other than arms. At present they don't have the national capacity to do so. They are a first class power only in their ability to destroy. He pointed to a real Soviet desire to reduce the arms race. Mr. Schulman noted the lack of a national constituency for disarmament in the United States.

Dr. Victor Alassi described the two foundations of the treaty—equality and ability to verify. SALT I placed some unequal upper limits on strategic arms such as ICBM, submarine launched missiles and long-range bombers. SALT II brings these limits down and gives equality between the two countries.

The ability to verify treaty provisions is the key to the treaty. The Soviet Union is a very closed, secretive nation. The U.S. clearly possesses many highly sophisticated methods for finding out what is being tested in the upper atmosphere, what large sites are being built and how Soviet resources are being allocated. It seems unlikely that a major weapon system could be developed without strong indication reaching the U.S. Because these methods are highly classified, only veiled hints of their effectiveness could be provided.

Each provision of the treaty must be cleared by the intelligence community before negotiations start. Ultimately the administration must be willing to certify that each provision can be verified. The treaty contains strong provisions against "blinding" satellite surveillance and purposeful concealment in other forms.

SALT II will run until 1985. Before then, negotiations will begin on SALT III which will take new technologies into account.

The final speaker was Dr. Frank Press, the President's Science Advisor. He appealed to the Science-Technical community for help in ratification of SALT II. He is persuaded that we possess the understanding, both of the destruction potential of the arms race and of the technical means for verification. Dr. Press noted the public-spirited efforts of the scientific technical community in areas of national policy such as environmental protection, reactor safety and recombinant DNA. Dr. Press noted, in passing, the commitment President Carter has made to basic research, including increasing funding 25%.

I left the briefing perplexed. Why had Dr. Press appealed to the Scientific Technical Community when he was unable to give us the life blood of our craft—data—data on verification? In my view, ratification should depend upon demonstration to the Senate that methods of verification exist and that unbiased and independent lines of evaluation are in place.

Ratification of SALT II should be viewed as taking one step backward from world annihilation, not solving all the problems between the U.S. and the U.S.S.R.
Contributions from Retired Members

The generosity of Retired Members whose contributions to the Society were received in 1979 is gratefully acknowledged. Listed below are those whose contributions were received by press time.

David I. Abramson
Harry F. Adler
Edward F. Adolph
Clarence M. Agress
J. Garrott Allen
Clifford Angerer
Sydney A. Asdell
Anna M. Baetjer
Leslie L. Bennett
Richard Bernard
Edward G. Boettiger
Walter M. Booker
Phyllis A. Bott
Emil Bozler
Pietro O. Bramante
Ellen Brown
Frank A. Brown, Jr.
George W. Brown
J. S. L. Browne
Austin M. Brues
Howard B. Burchell
D. Bailey Calvin
Aurin M. Chase
Herbert Chasis
Leon C. Chesley
J. Kapp Clark
Robert A. Cleghorn
Kenneth S. Cole
Julius I. Comroe, Jr.
Ruth E. Conklin
Andre F. Courmand
Francis N. Craig
Anonymous
Ray G. Daggs
Lewis Dexter
Frederick L. Day
William L. Doyle
Carl A. Dragsstedt
H. Hugh Dukes
Fwu Tarning Dun
Gustav Eckstein
Leonard H. Elwell
Carl F. Essig
Gerald T. Evans
Ernst Fischer
Louis B. Flexner
Francis M. Forster
Florent E. Franke
A. Stone Freedberg
Robert Gaunt
Charles F. Geis
Anna Goldineder
David E. Goldmacher
Holmut A. Gordon
Paul O. Greeley
Esther M. Greisheimer
H. Roberta Hafkesbring
Henry Haimovici
Reginald E. Haist
Henry B. Hall
John F. Hall, Jr.
Chester W. Hampel
A. Sidney Harris
Helen C. Harrison
Charles C. Hassett
Franz X. Hausberger
Frances A. Hellebrandt
Raymond C. Herrin
Alexander Hollaender
Joseph P. Holt, Sr.
Olive Huber
Ernst G. Huf
Jane Sands Robb Johnson
Frederic T. Jung
Fredrick W. Kinard
Barry G. King
George F. Koepf
Kenneth G. Kohlstaedt
Eszter B. Kokas
Robert W. Lackey
Eugene M. Landis
Charles E. Lane
Henry D. Lauson
John H. Lawrence
Samuel L. Leonard
Lena A. Lewis
David R. Lincicome
Donald B. Lindsay
Frederick W. Lorenz
Anonymous
Aldo A. Luisada
Eleanor D. Mason
Evan W. McChesney
Grayson P. McCouch
Fred A. Mettler
Augustus T. Miller, Jr.
James A. Miller, Jr.
David Minard
Hugh Montgomery
Dan H. Moore
Hayden C. Nicholson
Morton J. Oppenheimer
Elizabeth E. Painter-Marcus
Ernest A. Pinson
Samuel E. Pond
Walter Redisch
Emerson A. Reed
Richard K. Richards
Lorrin A. Riggs
Richard L. Riley
David McK. Riouci
Eugene Robillard
Louise P. Roquemore
Howard H. Rostoker
Leon J. Soul
Francis E. Saunders
V. Brown Scott
M. C. Shelsky
Miriam E. Simpson
Dietrich C. Smith
Falconer Smith
Samuel Soskin
George W. Stavrak
Anonymous
J. Clifford Stickney
Roy L. Swank
Katherine L. Sydnor
Oscar E. Tauber
Clara Torda
Anthonie Van Harreveld
Edward J. Van Liere
Kurt N. von Kauila
Owen I. Wangensteen
William A. Weber
Marion E. Webster
Floyd J. Wierciinski
Richard W. Whitehead
Harold C. Wiggers
William F. Windle
Charles A. Winter
William B. Youmans
John A. Zapp, Jr.
Raymund L. Zwemer
HONORS AND AWARDS

Two APS members were elected to membership in the National Academy of Engineering. The honor was conferred on those who have made important contributions to engineering theory and practice or who have demonstrated unusual accomplishments in the pioneering of new and developing fields of technology.

A. Pharo Gagge, John B. Pierce Foundation Laboratory and Professor Emeritus of Epidemiology, Yale University was honored for contributions to the basic principles of air conditioning and bioengineering of heat transfer in man.

Otto H. Schmitt, Professor of Physics and Biology, Dept. of Electrical Engineering, University of Minnesota, was honored for pioneering contributions in the development of bioengineering and biophysics and in the interdisciplinary science including vectorcardiography, bioelectricity, and electronic circuitry.

HIRAM E. ESSEX

Dr. Hiram E. Essex, President of the Society in 1954-55, died in Rochester, Minnesota on December 15, 1978, at the age of 85. Dr. Essex was elected to Council in 1941 and served almost continuously until 1956. He also served as a member of the Board of Publication Trustees.

INTERAMERICAN MEDICAL CONGRESS

The Spanish American Medical Society, a 50-year-old organization of Spanish speaking physicians will sponsor the III Interamerican Medical Congress in New York City at the Americana Hotel on October 5-8, 1979, celebrating "El Dia De La Raza" (Columbus Day).

The Faculty has prominent physicians from the Spanish speaking countries as well as American physicians.

This Congress has 20 hours’ credit for C.M.E. and will be held annually:
October 10-13, 1980
October 9-12, 1981
October 8-11, 1982
October 7-10, 1983

For further information, contact Dr. Rene F. Rodriguez, Chairman, 37-21 75th St., Jackson Heights, NY 11372

SPRING MEETING SYMPOSIA SUPPORT

The Society gratefully acknowledges the contributions received from various industrial donors in support of selected symposia organized for the Spring Meeting. These contributions were solicited on behalf of the Society by:

D. O. Carpenter
J. W. Manning
C. S. Nicoll
H. K. Orkand
K. Wasserman
K. T. Weber
C. N. Woolsey
J. A. Zadunaisky

Contributions in support of the symposia were received from:

Abbott Laboratories
Ayerst Laboratories
Beckman Instruments
Burroughs Wellcome Co.
CIBA Pharmaceuticals
CIBA — Geigy Corp. (Pharmaceuticals Div.)
Geigy Pharmaceuticals
JOLI, USA, Inc.
Anonymous
Hoffman-LaRoche, Inc.
Lilly Research Laboratories, Div. of Eli Lilly & Co.
Merck Sharp and Dohme, Inc.
Pfizer, Inc.
Roche Laboratories, Div. of Hoffman-LaRoche, Inc.
Sandoz Pharmaceuticals
Smith Kline & French Laboratories
Texas Instruments, Inc.
The Upjohn Company
Syntex Corp. (Syntex Research Div.)
The Squibb Institute for Medical Research
In April 1976 the reorganization of the Society journals was announced. At that time, it was anticipated that the number of new manuscripts submitted for the:

1. *American Journals of Physiology* (AJP) would increase, as certain areas formerly covered in the *Journal of Applied Physiology* were incorporated into AJP and two new journals were formed, i.e., AJP: Cell Physiology and AJP: Regulatory, Integrative and Comparative Physiology.

2. *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology* (JAP) would decrease, as the journal became more specialized.

3. *Journal of Neurophysiology* (JN) and *Physiological Reviews* (PRV) would remain unchanged.

Between 1975, before the reorganization, and 1977, the first full year after the reorganization, these predictions were followed reasonably well. The number of new manuscripts received per year increased by 43% for AJP, declined by 8% for JAP, and declined by 9% for JN. For these journals combined there was an increase of 19% (1869 to 2217). In 1978 the number of new manuscripts received was higher than in 1977 for each of the journals: AJP, +6%; JAP, +7%; and JN, +31%. For these journals combined there were two increases of 8%. Between 1975 and 1978 the changes were: AJP, +52%, JAP, -2%; and JN, +20%. For the journals combined, the number of new manuscripts received per year between 1975 and 1978 increased by 28% (from 1869 to 2400). This increase is greater than anticipated in 1976.

### Change in Number of Manuscripts Received

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<td>AJP</td>
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In 1978 the number of regular articles published increased by 5% over 1977; 11% over 1976. Editor's pages (pages used by Editors as best suit the needs of each journal) increased by 45% for AJP and 4% for JAP from 1977 to 1978. The total number of text pages published changed from 1977 by +11% (599) for AJP, -3% (76) for JAP, +15% (221) for JN, and -11% (96) for PRV. The overall increase in the number of pages published was 9%, i.e., 840 pages. Similar figures comparing 1976 (before the journals were reorganized) with 1978 are +56% (2086) for AJP, +3% (61) for JAP, +18% (257) for JN, and +17% (140) for PRV. In 1977 and 1978 combined, 4248 more text pages were published than in 1976. The increase in the number of new manuscripts received, and speedier reviewing and production (acceptance rate is somewhat lower) have permitted this phenomenal growth.

### Journal Text Pages Published

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1. Contents, indexes, etc.
2. Excluding cumulative index of 400 pages.
CASE HISTORY OF A PHYSIOLOGIST: F. G. HALL

D. B. Dill
Desert Biology Research Center
Department of Biological Sciences
University of Nevada, Las Vegas
Boulder City, Nevada 89005

Introduction

A symposium on “Physiological Adaptations: Desert and Mountain” was held in Las Vegas April 19 and 20, 1971. It was jointly sponsored by the Desert Research Institute and the University of Nevada, Las Vegas. The plan was conceived by Raymond J. Hock, professor, UNLV. After his untimely and tragic death it was brought to fruition by Mohamed K. Yousef, professor, UNLV. The symposium recognized my 80th birthday. I was invited to give the dinner address. My address honored my good friend and my colleague in many field studies, Frank Gregory Hall. The Desert Research Institute in 1971 printed my address for distribution to symposium participants and friends. In 1972 the Symposium Proceedings, edited by M. K. Yousef, S. M. Horvath and R. W. Ballard was published by Academic Press. In the years since 1971 The Physiologist has become a source-journal for history of the American Physiological Society. Since my lecture touched on the activities of many members of the Society besides those of Hall and Dill it has been submitted to the editor for consideration.

I remarked at the beginning that there was one whom I missed above all others at the symposium: Frank Gregory Hall—Greg. I reviewed his career hoping to create the feeling that he was one of us. As the story unfolds it will become evident that Greg and I had common beginnings and shared many experiences. Both of us were born in the rural midwest and started our education in one-room one-teacher country schools, and were orphaned young. Each of us lost a parent to tuberculosis. We had no brothers; he had three sisters and I had four. We both graduated from small colleges and received honorary doctorates from those colleges.

An account of his early years is given in some detail herein; his experiences of those years were imprinted for life. His graduate years included both joys and sorrows, and his 40 years at Duke University brought him great honor. I have enjoyed relating our experiences of six expeditions together to the desert, sub-tropics and mountains between the years 1935 to 1966, and during two years spent together during World War II in the Aero-Medical Laboratory. Since 1937 I have enjoyed the friendship of his wife Stephanie, his daughter Betty, and his son Kenneth who is now a professor at Duke University. All have helped me in this task, and Betty and Kenneth, I am happy to say, attended the dinner.

Birth To Manhood—1896-1917

Greg was born on February 12, 1896, in a small town of Johnstown Center in southern Wisconsin. His grandfather, Gregory Dexter Hall, was a dominant leader in the community of Johnstown Center. From his 1,000 acres of prairie, he gave land for the settlement, built the school, the church, the town hall, and a tall brick home from which he could view the town and his farm. From the house, Grandfather Hall sailed forth with his gold-headed cane; arrayed in a long frock coat, high silk hat, a long flowing black silk tie and a beard; he was an impressive figure. He died in 1906 when Greg was 10. His wife, Elida Austin, a granddaughter of President Tyler, died in that house in 1916 when Greg was 20 years old.

Greg’s parents, Frank Dexter Hall and Evaline (or Evelyn) Kidder, a school teacher, were married April 19, 1893. They settled in the “Center” where they owned the general store. The town was a more self-contained community than small towns of today. The town hall served for elections, dances, road shows and local entertainments. In back of the hall was a barn, a corral where farm stock was auctioned, and a stable for travelers’ horses. The general store sold everything but meat, and also served as a post office. There were rooms for the family and rooms to rent to travelers on the coach road between LaCrosse and Milwaukee; some of these Greg’s mother boarded.

Other buildings in the town included a Presbyterian church where Evaline played the organ, and a home for the minister, his mother and two unmarried sisters. Next to the church was Dr. William Rockwell’s home. As the horse and buggy doctor for the surrounding area, he performed surgery, set broken bones, and often pulled teeth in his living room. Next to the one-room school was a small house for the teacher. The blacksmith shop had rooms in the back for the family, and the slaughter house and meat market were beside the creek. Some distance across the creek was a sorghum mill and an apple cider mill. One-half mile away Greg’s Uncle Lee ran a dairy and cheese factory.

Marjorie, Mary and Elida, Greg’s three sisters, were born in Johnstown and all but Elida went to the one-teacher school. Marjorie and Mary have written interesting letters to me concerning the town. There was a swimming hole in the creek and in the winter they skated there. Mary related a family anecdote—it seems Greg was paid five cents a week to carry water from the well to the house. When he was 10 and Mary was 4, he subcontracted with Mary to carry the water for one cent a week, a profitable business for him.
Their father died of tuberculosis in 1905. Sometime earlier, however, he had sold the store and built a home nearby. Here they lived until 1907 when they moved to nearby Milton. Greg was then 11 and Elida, the youngest, was 3. In 1910 Evaline was remarried to Ed Hurley, a neighbor who had seven children of his own, five living with him and two away. Ed had relatives in central Nebraska and the family moved to a ranch five miles from North Loup. One bright spot for Greg lay in the fact that he had a pony to ride to the North Loup High School from the ranch. After the move, their mother took in washing to help support the family. Marjorie writes that her mother loved all the children. But she sent Greg back to Milton in 1911 to attend the Milton Academy. The following year, she died suddenly on October 12, and her three daughters accompanied the body back to Milton where she was buried beside their father. They then lived with their uncle's family, Mr. and Mrs. Otis Hall, who had a farm in Johnson County. Uncle Otis became their guardian.

At this time Greg was starting his last year in Milton Academy. After graduation in 1913, he entered Milton College. He often spoke of his happy years there. A fellow student, later Milton's chemistry professor, William Burdick, recalls that in his college days Greg "re corded the intellectual curiosity and originality which are essential to the success of a research scientist." Greg’s superiority in biology led to the appointment in his senior year as a biology instructor under the direction of Professor A. R. Crandall.

In the spring of 1917 he became engaged to a classmate, Beth Marie Davis, who was a granddaughter of one of the founders of Milton College. Greg’s sister, Marjorie, describes Beth as having been a wonderful person. Greg often spoke of his visits to his sisters, all of whom settled in Wisconsin. Marjorie graduated from Milton High School, the Whitewater Normal School and taught school there until her marriage to Joseph Weber, a farmer and carpenter. They settled in Dorchester, Wisconsin. Marjorie has been active in community affairs, particularly in those involving children. In recognition of this, she was listed in “Who’s Who in American Women” in 1957. Elida taught school in Dorchester for one year before marrying John Bohanyin. They had seven children; she died two days after the birth of twins on March 4, 1952. Mary, the second sister went to live with Marjorie in 1920 and in 1922 married Tom Johnston. There was a divorce a few months later, after which she was remarried to Joseph Christie who died in 1957. She lives at Chetek, Wisconsin. Mary and Marjorie have written interesting and informative letters to me about early days in Johnstown and about the family. I am indebted to them for the account of Greg’s background and early years.

Post-Graduate Years – 1917-1923

These years encompassed notable achievements, and both happy events and a major tragedy. Greg had been an instructor in biology in his senior year. He spent the summer of 1917 taking part in a biological survey of life zones and terrestrial vertebrates of Wisconsin. This was planned by Professor George Wagner and by Dr. Hartley H. T. Jackson who was in charge of the mammal collection, U.S. Biological Survey. Jackson had graduated from Milton in 1904 and sought a young Milton graduate to work with him – Greg was chosen. Greg often spoke of that summer’s work, his beginnings in research. Only a few years ago he mentioned discovering that some of the specimens he collected were still available in the National Museum. Jackson has written that Greg was “always a willing and capable worker and became one of my closest friends.” That summer Greg visited Madison to explore the possibility of pursuing graduate study at the University. The plan took shape in his mind, but remained dormant since he was committed to returning in the fall of 1917 to teach biology at Milton.

With the country at war, Greg enlisted in the Signal Corps in the spring of 1918 and was assigned to the Meteorological Section. Shortly he was sent to Columbia University for special training. On July 4, 1918, he and Beth were married in New York State; they had some time together in New York City. That fall he was transferred to the University of Texas for further training and Beth returned to Wisconsin to teach English at Watertown High School. Greg was proud of his service in the infant aviation organization which evolved into the Army Air Corps, later becoming the Army Air Forces and now the U.S. Air Force.

When Greg was relieved of active duty in the spring of 1919, Beth joined him in Milton. Soon they went to Madison where Greg began graduate study in the summer school. That fall they returned to Milton where Greg had been appointed professor of biology.

Their daughter, Betty, was born on May 12, 1920, but it had been a difficult pregnancy and Beth never recovered from the complications of childbirth. She died on May 30, 1920.

After this tragic loss, Greg went to Madison for graduate study, but before leaving he arranged with one of Beth’s first cousins, Margaret Post Bliss, to care for his daughter. Betty, now living in California, Betty writes that when her father went to the hospital on May 30, 1920, he found his wife dead and his infant daughter in precarious condition. Betty has been told that she was tiny enough to fit into a cigar box. It was with this desperate situation facing him that Margaret took Betty in hand. Margaret’s father, a doctor, predicted that the baby would not survive, but with feedings every two hours around the clock, she was saved. Eighteen months later Margaret Bliss (Aunt Marge) gave birth to her first child, also a daughter and the two girls became almost inseparable. Margaret’s husband became Dean of Engineering at Marquette.

Greg received the Master’s Degree in 1921 under A. S. Pearse. Chauncey Leake was then an instructor and graduate student. He and Greg published a paper together in the American Journal of Physiology which dealt with the regulation of vascular tone (31). Chauncey wrote that Greg was a serious, hard-working student, with a quick smile, a quiet way and solid intelligence. He says that Greg was a great teacher but a slow writer, and he urged Greg to “write more – but he would only smile.”

Greg’s doctoral dissertation, The Function of the Swimbladder in Fishes was started in the summer of 1921 while he was employed by the U.S. Bureau of Fisheries. His observations were made in Lake Mendota in the laboratory, and he demonstrated ingenuity in many phases of his experiments. Among his experimental designs was an apparatus for studying the effects of pressure on the composition of gas in the swimbladder. An iron pipe 8” x 36” was fitted with a cap at one end, and a four inch view window at the other. An inlet pipe supplied water to this tank from a reservoir on the 4th floor; the outlet pipe carried the overflow also to the 4th floor, 60 feet above the tank. By this means he was able to demonstrate that this increase in pressure applied for 10 hours raised the O2 in the swimbladder from 12.1 to 18.5%. He concluded that the primary role of the swimbladder is hydrostatic. While gases ordinarily reach the swimbladder by diffusion, in some species at least oxygen can be secreted into the bladder. The thesis was published in the Biological Bulletin (20), and reprints, in conformity with University requirements, were deposited in the library.

Greg had spent the summer of 1922 at the Marine Biological Laboratory (MBL), Wood’s Hole, Massachusetts, taking a
course in Invertebrate Zoology. A fellow student, I. E. Gray, was destined to become his lifelong friend. Greg persuaded Gray to apply for a teaching assistantship at Wisconsin; he was accepted and started his graduate study when Greg was finishing. They roomed together that year. Another associate, both at MBL and Madison, was Samuel Lepkovsky, who is now professor emeritus at Berkeley and is still busy in the laboratory there.

My first tie to Greg, though tenuous, was through Wisconsin. My first year in high school was in Washington, Iowa, where my stimulating teacher of physiology and botany, H. I. Case, boasted of being a Wisconsin graduate, class of 1890. My next three high school years were at Santa Ana, California where our highly respected principal and most able teacher of mathematics was Edward B. Oakley. He, like Case, had been a poor Wisconsin boy who earned his way through the University, graduating in 1879.

After receiving his doctorate in 1923, Greg returned to Milton as professor of biology. This was the beginning of a new era in more ways than one. He and Stephanie Daland were married that summer. Stephanie, a daughter of Milton’s president, had graduated in 1917 and then worked in the Racine library. She later attended and ultimately became a staff member at the library School at Madison which eventually became an integral part of the University.

Margaret Bliss and her husband wanted to adopt Betty, but all accepted Stephanie’s decision that Betty should be with Greg and her. Margaret says that after separating the two girls her daughter “did not eat for a year.”

Betty graduated from Duke University in 1947. She sang in the glee club and choir and sings in her church choir now. A month after graduation she married a classmate, Kent Boutwell. He obtained a Ph.D. in mechanical engineering at the University of Michigan and taught engineering there for 12 years. He is now a research scientist with General Motors Research Laboratory in Santa Barbara. (By an extraordinary set of coincidences, my daughter’s name is Betty; she too lives in Santa Barbara, and her husband is also a scientist. Betty Boutwell has four children; my daughter has three, and all of the children are in the same age range.

At Duke University - 1926-1967

Greg’s mentor at Wisconsin, A. S. Pearse, had accepted Duke University’s offer of a professorship of zoology, with the responsibility for graduate study in zoology. His acceptance of this offer was contingent upon completion of a sabbatical leave and appointment of a suitable assistant. With the experience of three years on the Milton faculty behind him, Greg was invited to become associate in Zoology at Duke. He, Stephanie and Betty arrived in the fall of 1926, and Pearse arrived at the beginning of the second semester. They made a great team of teachers and investigators. Within a short time, two of their graduate students were awarded Ph.D.s, the first of these degrees to be awarded in the young university. Both Pearse and Greg enjoyed life on the full and both had a keen sense of humor. One of the many tales about Pearse occurred during the latter part of the war when I had persuaded him to act as a consultant to the Army Quarter-master Corps. Even he, a professor and a Harvard Ph.D., was required to complete a questionnaire concerning his personal life. To the question, “Have you ever been discharged from a position?” he wrote, “At age 10 I was fired from my one dollar per week job as delivery boy for a grocery store.”

This was an eventful year for the family. Kenneth was born on October 26 of that year. I became acquainted with Kenneth and Betty when I visited Durham in 1937 after our desert study. When Greg brought his family to Dayton during the war years, Kenneth was active in the Boy Scouts. After graduating from Duke University in 1949, he entered the Duke University School of Medicine, and interned in surgery-obstetrics-gynecology at Rochester, N.Y. After his internship, he received special training in anesthesiology at Duke and in the National Institutes of Health as Chief of the Section on Pain. He then returned to Duke where he was appointed assistant professor of anesthesiology in the Department of Surgery. In 1968 he was appointed to a professorship in that department.

Kenneth found time to work with his father in the laboratory, and between 1951 and 1966 they co-authored three papers. In 1964 he accompanied Greg when they participated in our desert study (details of which are discussed in a later section). Kenneth and Maidi Ebel became acquainted in Rochester where her father was an eminent physician. After their engagement, Kenneth had to resist urging by her father to join him in the general practice of medicine. But Kenneth had already determined on a career in research and medical education in anesthesiology. This he has achieved. He and Maidi and their four children are happy in their home near the University.

During their first year at Duke, Pearse and Hall completed a book entitled, Homiothermism, the Origin of Warm-Blooded Vertebrates (36). A part of their preface defined the scope, “The physiological and ecological aspects of one type of adjustment which has made successful life on land possible and has reached its climax in the attainment of thermal and chemical stability within the bodies of animals.”

In 1929-30, Pearse was visiting professor at Keio University, Japan; he left Greg with responsibility for recruiting more scientists for the department. The new recruits were George Iaggart from Syracuse and his friend from graduate days at MBL and Wisconsin, Gray from Tulane. The Halls and Grays were best friends and next door neighbors for years.

Greg’s progress up the academic ladder was rapid. In 1930 he was promoted to a professorship, and during this period Pearse and many colleagues at Duke, including Greg, founded the Marine Laboratory of Duke University at Beaufort, North Carolina. This is owned and operated by the University. Greg gave a course in physiology there one summer and gave the A. S. Pearse Memorial Lecture there some years ago. In 1932 Greg and others went with Pearse to Yucatan to study cenotes. This expedition will be discussed later.

Of major importance to Greg’s future was his sabbatical year with Barcroft which began in February of 1933. As an investigator, he brought great talent to bear on the problems of respiratory physiology that were concerning Barcroft at the time. With Barcroft, Greg co-authored a paper on fetal circulation and had a related paper of his own (21). During that year he also became acquainted with Bryan Matthews and a young physiologist from the U.S., Ancel Keys. They were to be together in 1935.

Stephanie writes that she took Betty and Kenneth to their mother’s home in Milton late in January. The first night the temperature dropped to 18° F., quite a contrast to the mild climate of Durham. Stephanie joined Greg in July when his studies were nearly completed.

Those weeks were memorable. They were entertained by the Barcrots, the Matthews and the Adairs. Their travels took them to Stratford-on-Avon to see a Shakespeare play and to visit historic sites in London, Edinburgh and Paris. Greg, an expert photographer, brought back many pictures. They returned on the Berengaria and were reunited with Betty and Kenneth.

The next summer found Greg back at MBL. In the fall he visited the Fatigue Laboratory to help plan the high altitude study...
of 1935. Also, he was a subject in the control studies, particularly in properties of arterial blood. Accounts of the 1935 study, the Yucatan expedition, our desert study of 1937, our Mississippi study of 1939 and the post-war expeditions to mountains and desert in 1962, 1964 and 1966 will be given later.

A major event in the family history took place in the winter of 1939-40: the building of their beautiful home which is set in the pines and dogwoods that cover the hills around the University. It is a tribute to Greg’s devotion to his country that less than a year after the home was completed, he took leave of absence for military duty at the AeroMedical Laboratory (AeroMed). Stephanie remained at Durham until 1942 when she and Kenneth joined Greg at Dayton. They were fortunate to have responsible military families renting their home during the war years.

Upon his return to Duke, Greg was asked to become a Professor in the Department of Physiology and Pharmacology in the School of Medicine. He had a busy life during the post-war years. Contracts with the Air Force enabled him to equip a small laboratory away from the department. Here during weekends and summers he continued his research on hypoxia, with particular interest in respiratory function. Two assistants who joined him at AeroMed were Kenneth Penrod, who arrived in 1950, and Wayland Hull, who came later. Penrod turned to administrative tasks and is now Vice Chancellor for Medical Affairs at the State University System of Florida. Hull is now assistant to the Medical Director, Manned Spacecraft Center, Houston.

Our common interest in aviation medicine occasionally brought us together, as on November 12, 1948 when Major General Harry Armstrong, then Commandant of the School of Aviation Medicine at Randolph Air Force Base, assembled investigators, including Greg and me, in the field of aeromedical research. This pioneer inquiry was titled “First Panel Meeting on AeroMedical Problems of Space Travel.”

A year later Greg and I shared a notable experience in Lima, Peru. Professors Carlos Monge and Alberto Hurtado and their associates arranged a symposium on the Biology of High Altitudes (51). One feature was the dedication of the new high altitude station at Morococha (14,900 ft.). The Air Force had helped support their research; this involved Major General Armstrong and Brigadier General Benson who arranged to transport a party of scientists to the symposium. Included in the group were Brigadier General Wallace Graham (the White House physician), Wallace Fenn, Joseph Kaplan, Randolph Lovelace, Ashton Graybiel, Albert Behnke and others. Other Air Force representatives were Major Cain and Harry Adler (see Figure 1). It had been 14 years since Greg and I had visited Lima incident to our high altitude study in Chile. Following Hurtado’s example, many students had spent a year in the U. S., including two, Juan Aste-Salazar and Leon Contreras, who had come to the Harvard Fatigue Laboratory. The symposium was a great success, culminating in the dedication of the laboratory at Morococha.

A caravan was assembled to take the visitors by car up nearly 15,000 feet in three hours. A rank order was adopted which placed Harry Adler, Greg, the scientific attaché of the Embassy of Mexico and me in car 14. Adler sat with the driver who disliked being 14th in line, before long he had passed cars 13 and 12, despite the many hairpin turns. Adler’s remonstrances only spurred him on. I remarked to the driver that his friends must call him “el tigre,” to which he replied, “si, si, senor.”

The Mexican and I carried on a worried conversation, but decided we could only hope for good luck. Greg, who sat between us, showed no sign of worry, but he did not engage in conversation. The Mexican could not draw him out and at length characterized him aptly, “El hombre del pocas palabras,” the man of few words! When we reached the summit we were No. 31. As soon as all had arrived we were escorted to a railroad dining car for lunch. I sat with Behnke, Graybiel and Greg. Behnke, proud of his physical fitness, began bantering Graybiel, but before the meal was finished Graybiel, who was enjoying it, was delighted that mountain sickness had overcome Behnke. He was quite green when he left the table.

Fig. 1. In the Canal Zone, November, 1949, enroute to an International Symposium on the Biology of High Altitudes held in Lima, Peru. Left to right: Wing Commander J. C. Scott, Commander Simon Wesley Eyer, Captain Albert Behnke MC, Dr. Ulrich Luft, Captain Ashton Graybiel MC, Brigadier General Wallace Graham MC, Dr. Harry Adler, Dr. Shields Warren, Dr. Randolph Lovelace, Dr. Wallace Fenn, Dr. F. G. Hall, Captain Wilbur Kellum MC, Major General Harry Armstrong MC, N. Scott, Dr. Sam Geften, Dr. Joseph Kaplan, Brigadier General Otis O. Benson, Jr. MC, Dr. Bruce Dill, Major C. G. Cain.

Otis Benson recalls that the party spent the first night at Huancayo (12,000 feet) and that we were much more sedate after a sleep interrupted by Cheyne-Stokes breathing. He also recalls the risky return trip—across every hairpin turn bare witness to the low value Peruvian drivers place on life.

Before the symposium adjourned, we decided to entertain our hosts at a banquet at La Lagunrta in Callao, Lima’s seaport. Captain Wilber Kellum and I were delegated to arrange the seating, but I left most of it to him, an expert in protocol. We invited the wives to the party, an unusual and happy experience for them (it seemed their husbands considered their place was in the home). In another part of the large dining room we discovered the current Miss Mexico was being entertained. One of our dashing guests decided Major Cain was the shiest person present; Miss Mexico was easily persuaded to ask him to dance, an experience I daresay he still has not forgotten. I am constrained to describe these experiences in Peru since they constituted one of the elements that bound our lives together.

In the early 1950s the Navy decided to seek a civilian scientist to direct research at its Aviation Medical Acceleration Laboratory at Johnsville, Pennsylvania. Greg received an invitation to apply for the position; the lengthy personnel forms were attached. Shortly after he declined, he had a telephone call from an admiral who asked for a date to discuss the matter. The date was set, Greg listened quietly to the Admiral’s eloquent proposal, and then shocked him by declining again. When the Admiral renewed his plea, pointing out the big increase in pay, the liberal retirement plan and fringe benefits, Greg took him to the window of his office. “There is the reason for my decision,” he said. The admiral was not impressed by the beauty of the campus nor by the many students on their way back to classes. “Dr. Hall,” he said, “if that is what is holding you back, I’ll promise to have a
platoon of marines march past your window every hour on the hour." The admiral left, still not appreciating Greg's point of view.

For several years I saw Greg only at meetings. In 1955 the fall meeting of the American Physiological Society was held at Tufts College, Medford, Massachusetts. There I heard about the vicious mugging Greg had experienced in March of that year. At dusk he was starting up the steps to the emergency entrance of the Duke Hospital when he was struck over the head with a heavy, blunt instrument. He did not collapse and his assailant, realizing this, ran off—but not before Greg had noticed that he was a stranger. Greg walked into the emergency room for help without realizing that blood was streaming down his face from the deep head wound. He was given first aid and was hospitalized overnight. There seemed to be no residual effects beyond emotional shock, but it seemed to me that Greg was shaken by the memories aroused through the telling of this experience.

Greg made what proved to be an important decision in 1956 when he had John Salzano appointed to his staff. John had received his doctorate that year at the University of Iowa under Wade Tuttle. Steve Horvath, then at Iowa, introduced John to Greg. At that time Fred Zechman, Jr., was with Greg as a post-doctoral fellow, having received his doctorate with Greg the year before. The three worked together on studies of the role of the vagus nerves in pulmonary mechanics. The next year Fred left, and he is now head of the Department of Physiology and Biophysics in the School of Medicine, University of Kentucky. June Barker returned to join the group after a year's study in England. Those were busy days, teaching several groups of students physiology and pharmacology. However, with Air Force support, Greg and John were active in aeromedical research, particularly in the summer months. Medical students were employed as assistants. John writes that, as chairman, Greg took a personal interest in the members of the department and in the execution of his responsibilities as department chairman.

In 1960 I was selected to edit a volume of the Physiological Society's Handbook. This became Volume 5, *Adaptation to the Environment*. I invited Greg to write a chapter, but he replied: "I regret that I had better not take on one of the chapters. I have committed myself to a heavy load of work here at Duke for the coming year. I feel that I shall not have the time for contemplation that would be required for writing. I also find it much harder to write as I get older. I shall, of course, be very glad to help on any of the details. I have made a few suggestions as to possible authors of chapters."

From 1961 we corresponded frequently about our studies together of the physiology of mountain and desert, details of those studies will follow. In June, 1965, he retired at the mandatory age of 69. He was then free to follow his own desires and was happy in his laboratory with John Salzano. His interests during this period were concerned with respiratory function of the blood in rodents. Among several papers in this field, one dealing with hemoglobin and oxygen affinities of seven species of squirrels was published in *Science* (23).

Many honors came to Greg during his years at Duke. At the close of the war, besides the Legion of Merit (see World War II), he received letters of appreciation from Major General Grant, the Air Surgeon, and from Detlev Bronk. Bronk was scientific advisor to the Air Force during the war, and later was president of Rockefeller University. Greg was honored in June, 1957, by his alma mater, Milton College, by the award of an honorary degree of Doctor of Science. In 1966 he was elected a Fellow of the Aerospace Medical Association in recognition of his many achievements in the field of Aerospace Medicine. Crowning recognition came in the fall of 1966 with a dinner honoring his 40 years of service to Duke University. This was held at the Hope Valley Country Club and about 100 of his friends and associates were in attendance. My wife and I were privileged to be there. His portrait was presented and now hangs in the Physiology Department of the Medical School.

**WORLD WAR II-1941-1945**

In the summer of 1940 Greg spent some time at the Fatigue Laboratory studying, with Otis Benson, Will Forbes and me, respiratory regulation in oxygen lack as affected by amphetamine (I). Otis, then a captain in the Medical Corps, was soon to relieve Harry Armstrong as chief of the AeroMedical Laboratory, Wright Field. This will be referred to subsequently as AeroMed. In preparation for this assignment, Benson spent some months with us and at the Mayo Clinic. He convinced Greg and me that we should apply for commissions to assist him in expanding the research program at AeroMed. This we did, looking forward to six months in uniform and the subsequent return to our universities.

Greg and I arrived at AeroMed early in January, 1941. I had been commissioned a major in the Specialists Corps as it was then called. In April, 1942, Greg was also commissioned. Aero Med was familiar to me. Sid Robinson, Harndt Edwards and I had collaborated with Harry Armstrong and John Heim in 1937 when Harold and I were on our way to Boulder City (I). At the time, the new altitude chamber had just been completed and we conducted the first experiment in it.

Benson's vision of unchartered fields is illustrated by the fact that he introduced anthropometry to the military services. During the summer of 1940, he sought the advice of Ernest Hooton, Professor of Anthropology at Harvard. Growing out of this discussion, four of Hooton's students measured Air Force cadets and gunners for purposes of equipment design. After Hooton had analyzed their results, two of the students, Albert Damon and Francis Randall, were commissioned and assigned to AeroMed to apply Hooton's statistical data. They remained there during the war as members of Pharo Gagge's Biophysics Branch. Randall was killed in an airline accident; Damon became a member of the Anthropology Department at Harvard. Their research has played a major role in the redesign of clothing, footgear and other items of personal equipment developed for military use.

Benson said we must have a biophysicist and sometime later Pharo Gagge was persuaded to fill this role. We found a strong nucleus at AeroMed that included John Heim, John Hall and Ernie Pinson. Ernie had received his Ph.D. at Rochester in 1940. He rose through the ranks to Major General and became Commander of the Air Force Institute of Technology at Wright Patterson Air Force Base where he began his career. Others who were recruited as lieutenants included "Ken" Penrod, Loren Carlson, Harvey Savely, Clarence Maaske, George Maison and John Wilson. Some, such as Ross MacCardle, came as civilians and were commissioned later. Our six months were stretched to twelve and Pearl Harbor found us ordered to remain on duty for the duration.

At the Fatigue Laboratory Will Forbes was displaying master craftsmanship in building up an outstanding group of investigators for attack on physiological problems of the military: cold, heat, protective clothing, footgear, load-carrying equipment and rations. I left Harvard with a strong group working with Will: Bob Darling, Lucien Bronha, Steve Horvath, Charlie Knehr and Frank Consolazio. Steve had already become my son-in-law. Shortly Will recruited Edgar Folk, II. L. Delding, Don Griffin, Paul Robinson and Ann Hoyt. Later Sid Delding brought his stu-
and would have died had they been in flight. Greg played a major role in our study of mask leakage. At 30,000 feet the system should supply the wearer with pure oxygen; a leak means that he inspires a gas mixture containing nitrogen. Determining the percent of nitrogen in the air in the mask during inspiration gives a basis for calculating the percentage of leakage since air contains about 79% of inert gas. For this purpose Greg adapted a device described by Scholander (38). Five ml of gas was drawn from the mask into a calibrated syringe. The gas was injected through pressure tubing into a burette. The bulb held about 40 ml of oxygen absorbent. Its upper end was a small bore tube, capacity 5 ml calibrated to read 1 to 100. The lower end of the burette was connected with pressure tubing to a leveling bulb containing mineral oil. The gas sample was shaken with the oxygen absorbent for one minute; then the remaining bubble was allowed to rise into the calibrated portion. With a minor correction, the reading corresponds to percent nitrogen in the sample. Since air is about 4/5th nitrogen, the percent leakage is 5/4ths the percent of nitrogen in the sample. Greg demonstrated that the method could be learned by young officers responsible for oxygen equipment in the field. This apparatus was procured and supplied to air bases; it was called “Unit Oxygen Officers Test Kit.”

Greg and I made many observations on respiratory responses to altitudes ranging up to 44,000 feet. We reported that at this altitude breathing pure oxygen is roughly equivalent to 18,000 feet breathing air (12).

Greg and I also tried out rations designed for emergency use. For emergencies, a 1-lb. bar of semisweet chocolate was available for air crews after bailing out. We were led to evaluate this when General “Hap” Arnold sent word from the Pacific that survivors of air crashes reported that this bar “looks like hell and tastes worse.” So we obtained some bars for trial. Although this when General “Hap” Arnold sent word from the Pacific that survivors of air crashes reported that this bar “looks like hell and tastes worse.” So we obtained some bars for trial. Although this, they were astonished to learn that we had been poisoned by theo- bromine. Pharmacologists could have predicted this, since they were aware that one pound of chocolate eaten within 12 hours raises the amount of the theobromine in the body to toxic levels. The D-bar soon was de-standardized.

At this time the K-ration had been developed by the Quartermaster with the advice of Ancel Keys. Greg and I decided to test this and, simultaneously, a pemmican ration which was under development at Wright Field. Pemmican was used by Indians long before the white man came to America. It was commonly made of dried berries and dried meat pounded together and packaged in animal casings. The pemmican we were to test was a nutritionally supplemented mixture derived from meat and grain products in powdered form. We were told that one small can held a day’s ration, and that it could be eaten dry, mixed with a little water to form a sludge, with more water to form a slurry, or with still more to form a beverage.

With Sergeant Murphy and a squad of soldiers, Kenneth Penrod, Sid Robinson, Gene Turrell, Greg and I undertook to evaluate pemmican and the K-ration. We went by C-47 to Albuquerque and in a short time with a light pack started across the desert for the Sandia Mountains. We opened the cans at noon; some ate part of the dry powder, but most decided to wait until evening. At our camp in cottonwoods on the banks of the Rio Grande we started eating the pemmican. Sergeant Murphy’s soldiers rebelled before they had downed much of it. So Murphy, a well-disciplined soldier, added enough water to his to make a slurry and quickly drank it; in minutes he appeared green and then vomited. Thus ended the trial of pemmican.

Previously an expert who had developed it reported he had tried some on the end of a knife blade. “It isn’t tasty,” he had said, “but a soldier could eat it if he had to.” We then lived on K-ration quite successfully for six days.

Greg and a driver were responsible for logistics, meeting us each night with blankets as we walked past the Santa Ana Pueblo into the mountains, past the Jemez crater and down towards Santa Fe. Before each evening meal Sid took blood samples for sugar analyses. Each morning three packages that constituted the day’s ration were issued. In the evening each listed and commented upon the uneaten items. All had comments to make but one, a soldier from the Kentucky hills with little education. When we pressed him for an explanation, he admitted it was less punishment to eat everything than to write about what he had not eaten.

At the end of six days we boarded the truck and covered the remaining miles to Santa Fe, stopping on the way for a visit with my friend, Wo Peen, an artist at the San Ildefonso Pueblo with whom I had become acquainted in 1937. After a big meal in Santa Fe, we continued to Albuquerque and soon were on our way to AeroMed.

Greg and I took part in one other field study while I was at AeroMed, a winter study at Oscoda, Michigan, of cold weather clothing, especially foot gear. The soldiers joined Bob Johnson, Will Forbes and me in a 23-mile march; not all of them finished the march with us.

Our reports concerning the poor performance of some oxygen equipment in the altitude chamber irritated some of the engineers at Wright Field who had shared the responsibility for its development. When the Office of Air Surgeon urged that responsibility for developing oxygen equipment be transferred to AeroMed, the engineers agreed provided Dill had no part in the plan. Colonel Doriot of the Quartermaster General’s Office requested my transfer, and it was quickly arranged. In April, 1943, Greg and I parted, meeting only infrequently during the remaining war years.

At about this time, Benson, then a colonel, replaced Colonel Armstrong at the School of Aviation Medicine at Randolph Field. Each became a major general and they both now live in retirement at San Antonio, Texas. W. Randolph Lovelace succeeded Benson at AeroMed; after the war he became Director of the Lovelace Clinic and Research Foundation in Albuquerque. He assembled a distinguished group, including Sam White and Ulrich Luft who attended my birthday dinner. Randy’s death in an aircraft accident in 1965 was a tragic blow for the Foundation and for aerospace medicine.

Greg continued to be concerned not only with familiar problems but also with the effects of acceleration and protection against it. His advice was invaluable in the design of “G” suits, for this he was awarded the Legion of Merit. Another interest,
allied to his biological background, lay in hydroponics. Raising vegetables in water containing essential nutrients seemed useful to rocky outposts such as Ascension Island in the South Atlantic. A system had been developed by the end of the war. Indicative of some of Greg’s responsibilities at AeroMed are three publications (25, 26, 27).

Late in the war, Greg had become the leading authority on many of the human problems of high altitude flight. Between February and April, 1944, his advice was sought by the European Theater of Operations, as a result of which he reached England in February to confer with General Grant, Colonel Armstrong and former associates from AeroMed, including George Maison and J. J. Smith. He had an opportunity to visit Cambridge where he renewed his friendships with Adair and Adrian and visited the laboratory where he had worked 21 years earlier. Greg was fond of telling about meeting the diener who had been the major domo of the laboratory for a long time. Evidently time had telescoped for he remarked casually to Greg, “You have been away some little time.” From England Greg went to North Africa and Italy where Otis Benson was the ranking Air Surgeon. He discussed problems of oxygen equipment and clothing with many officers and air crews. At the 26th General Hospital he was invited to give a lecture on problems of aviation physiology.

His next overseas duty took him to India in July and August of 1945. Again he was called upon to answer questions about oxygen equipment. His notebook records on August 2 that he had made 200 tests on mask leakage using the kit he had developed for that purpose. He must have been happy to find no mask with a leakage greater than 6%.

Many physiologists visited AeroMed during the years, contributing greatly to the research program. Besides those mentioned, I can think of Walter Ronthoff, F. J. Raides and Arthur Bulbulian of the Mayo Research Foundation; Glen Millikan, then at the University of Pennsylvania; Wallace Fenn from Rochester; Sid Robinson, Indiana University; David Tyler from Cal Tech; and F. J. W. Roughton, Cambridge. Experts who came to exchange ideas included Paul Siple, Lindbergh, Doolittle, and the surviving member of the Wright Brothers team, Orville. A monument to the Wright Brothers’ first flight stands on the hill above AeroMed.

Greg was relieved of active duty (but remained a reserve officer) in the fall of 1945, and returned to academic life at Duke University. He received from General T wing the highest non-combat award, the Legion of Merit. The citation reads: “His brilliant work in solving the many complex problems of human physiology in relation to flying reflects great credit to himself and the military service.”

Expeditions: Yucatan-1932

In 1932 Greg was a member of a group organized by Pearse to study the cenotes of Yucatan (35). Their report was published by the Carnegie Institution of Washington in 1936. The principal authors were Pearse, Creaser (University of Michigan), and Hall. Chapters were written by 14 collaborators dealing with life in cenotes. Greg’s chapter was entitled, “Physical and Chemical Survey of Cenotes of Yucatan.”

The peninsula of Yucatan consists of porous limestone covered with a thin layer of soil; there are no rivers over most of the peninsula. From ancient times the Indians have depended on cenotes for water. In some of them the water is one or two meters deep, but in many it is more than 20 meters deep. Greg observed transparency, gradients of temperature, pH and contents of CO₂, dissolved O₂, fixed CO₂ and chloride. He considered the belief held by some that subterranean rivers supply water to cenotes, but doubted that idea. It seemed likely to him that water enters through the porous limestone.

High Altitudes-1935

The International High Altitude Expedition of 1935 in which Greg played a major role was organized by Ancel Keys. In 1933 he was appointed an instructor and a tutor in biochemical sciences at Harvard after three years divided between Copenhagen with Krogh and Cambridge with Barcroft. While at Copenhagen, Ancel and Hohwü Christensen worked together under Krogh. They published a paper with him dealing with the organic metabolism of sea water (30). Ancel had discussed his dream of a high altitude study with Krogh and Barcroft and found them receptive. At Cambridge he had formed a close friendship with Bryan Matthews, then a graduate student at Cambridge and an enthusiastic mountaineer. Greg’s year at Cambridge overlappedAncel’s study there; Greg’s rich experience in respiratory physiology made him an obvious choice. Hohwü Christensen came as a Rockefeller fellow from Krogh’s laboratory to spend 1934-35 in the Fatigue Laboratory; he was eager to join the group. By the summer of 1934 plans were taking shape. Forbes and Edwards of the Fatigue Laboratory and McFarland, then of Columbia University, were signed up and sources of support were found.

The first site tentatively selected was the Pamirs. After two requests for authority were ignored by the USSR Embassy, the goal became Karakorum. Approval by British authorities seemed routine. Keys, Edwards and Forbes put together a field laboratory securely packaged in plywood cases suitable for porter transport. In December Keys left by air for India via San Francisco to make advance preparations, and Forbes left for New York to oversee loading laboratory cases, camping, sleeping and mountain climbing gear aboard a freighter bound for Karachi.

Before Keys reached San Francisco, a cable came from Barcroft to Henderson with the news that the authorities had refused permission for the expedition. Henderson acted at once, recalling Keys from San Francisco and asking Forbes to have the equipment unloaded and stored. Henderson, Keys and I reached the Fatigue Laboratory and McFarland, then of Columbia University, were signed up and sources of support were found.

An advance party, including Keys, Hall, Forbes, Edwards and Christensen, left in March by Grace Line for Antofagasta (see Figure 2). Matthews joined them two weeks later. Hastings had accepted a professorship at Harvard; in his place he recommended his associate, E. S. C. Barron (Achito), a biochemist from Peru, a graduate of the Medical School in Lima, and a protege of Carlos Monge, a distinguished scholar. Achito had come down from the hills to the University and Medical School. A poor Indian, his had been an uphill battle, but in medical school he had become a leader of his fellow students. At one time he led a strike demanding that professors give more time to teaching and less to private practice.

In late April, the second group left via Grace Line; these included McFarland, Talbott, Barron and me. Barron proved his value early, enlivening the stopover in Panama with a dinner and evening he had arranged at his cousin’s home, and at Lima, introducing us to his former chief, Carlos Monge, Professor of Medicine. We disembarked at Tocopilla and traveled by car to Chuquicamata, the great copper mining camp owned by Guagenheim interests.

The advance party had made good use of their six weeks.
Details with photographs are found in Keys's paper (28). It is of great credit to Keys that once he accepted the decision to shift from India to Chile, his great administrative skill, enthusiasm and initiative provided the basis for a successful expedition. With the help of the others, he had secured four rail cars: a cocina (kitchen car), a sleeping car of ancient U.S. vintage, a modern steel boxcar (our laboratory), and a flat car on which was mounted the body of a small boxcar, which was to become Greg's domain—a laboratory with quarters for animals.

For studies in comparative physiology, Greg had purchased a sheep, two rabbits, two ducks, a llama and a young vicuña. Later, at Ollagüe, he acquired two huallatas (a native goose), and a native relative of the ostrich, a rhea. Barron, Edwards and I helped him with blood studies on these animals, especially at the higher altitudes. He was senior author of the paper, “Comparative Physiology at High Altitudes” (24) that won him acclaim. It turned out that in several species native to high altitudes, when hemoglobin was examined in its natural medium, the red cells surrounded by plasma had greater affinity for oxygen than did the hemoglobin of their relatives native to sea level. Also, the llama and vicuña, both members of the camel family, had unusual red cells in that the hemoglobin was more tightly packed and the water content was less than in other mammals. Red cells of man and of most mammals contain about 335 g of hemoglobin per liter, for the llama, the figure is 439, and for the vicuña, 426.

Greg frequently demonstrated his great skill in handling instruments under the trying conditions he encountered, such as no running water, only a small motor generator as a source of power, a wide diurnal range in ambient temperature, and increasing hypoxia as our work took us into the higher altitudes. He not only had the intellectual qualities that enabled him to plan and carry out significant experiments, but he had the intellectual capacity to analyze and digest the findings. Greg was a subject in these studies and his work was invaluable. A summary of significant observations is shown in Table 1.

Values for Hall's arterial blood in most instances were close to the means. His serum Na generally was low and his serum K generally was the highest. It is worth emphasizing that his values for arterial pO₂ and % HbO₂ were as high or higher than the aver-
La Paz. I returned alone via Achito stopped over for a week to study acute mountain sickness, and Greg, Will and I continued. We put in at Quito for a day afterwards, Achito, Greg and Will Forbes. At Lima Edwards and kinkajous. This is a nocturnal mammal with a prehensile tail; it is absence. Then Achito had to retrieve Hohwti's paper money-drunken gringo friends and returned the money. Greg and I often were ready. Only in the last minute was Achito able to persuade Indian onlookers. They understood the error; they liked their under the influence of too much wine he had given it all way to the daughter of the Bolivian Consul to issue visas in her father's board, but the lieutenant ordered him to wait until his friends arrived before the last course; the engineer tried to persuade us to the restaurant was a gala affair. Each in turn proposed a toast followed by "seco" ("bottoms up"). The toast was translated by gasta and the others planned a visit to La Paz, Bolivia. But before Keys and Matthews were to return the equipment to Antof ono, resident workmen, it seemed that the displacement seen in the warm thick air of Ollague. There our party was to divide. Ourselves was a transient phenomenon.

All observations were completed at the camp and at Quilcha by July 15. We packed up the apparatus and returned by truck to the warm thick air of Ollaguel. There our party was to divide. Keys and Matthews were to return the equipment to Antofogaesta and the others planned a visit to La Paz, Bolivia. But before departure, we were entertained by our engineer friends and by the local lieutenant of the state police. The farewell banquet in the restaurant was a gala affair. Each in turn proposed a toast followed by "seco" ("bottoms up"). The toast was translated by Achito, including another "seco." The weekly train for La Paz arrived before the last course; the engineer tried to persuade us to board, but the lieutenant ordered him to wait until his friends were ready. Only in the last minute was Achito able to persuade the daughter of the Bolivian Consul to issue visas in her father's absence. Then Achito had to retrieve Holwell's paper money—under the influence of too much wine he had given it all way to Indian onlookers. They understood the error; they liked their drunken gringo friends and returned the money. Greg and I often reminisced about those days and nights together; the details never faded.

Our party broke up in part at Ollaguel and more completely at Quilcha. I returned alone via Lake Titicaca, Puno, Ariquipa and Molleindro where I hearted our Grace Line ship, meeting Edwards, Achito, Greg and Will Forbes. At Lima Edwards and Achito stopped over for a week to study acute mountain sickness, and Greg, Will and I continued. We put in at Quito for a day where Will bought a dugout canoe and Greg bought a pair of kinkajous. This is a nocturnal mammal with a prehensile tail; it is about the size of a cat. Will can tell incredible tales about their transport to New York, from the dock to the train. Eventually Greg reached Durham and he kept the animals in his laboratory there for several years. They did not reproduce.

### Desert Study—1937

Greg and I were together at Boulder City in 1937, his first study in the desert and my second. Our goal was to learn more about acclimatization to desert heat, particularly as related to rate of sweating and sweat composition. Our colleagues during the month's study were Edward Adolph, Harold Edwards, Frank Consolazio and for short periods Ross MacFarland and my son David, then 18. Adolph and Greg had joined the rest of us for control studies at the Fatigue Laboratory during the winter of 1936-37. We reported the results of observations on sweat rate and composition and described in detail the procedures (15). Winter sweat was about twice as salty as that produced after acclimatization to desert heat. Potassium in sweat remained nearly constant, while sodium and chloride concentrations varied with rate of sweating, with acclimatization and with the individual. The difference between individuals was marked. Analysis of my own showed the most salt, more than twice Greg's, and his was the most dilute while my son's was nearly as salty as mine.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>HbO₂</th>
<th>HbO₂</th>
<th>total CO₂</th>
<th>pCO₂</th>
<th>(Protein)</th>
<th>IC1₁₅</th>
<th>Na₁₅</th>
<th>K₁₅</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sea Level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>9.00</td>
<td>95.5</td>
<td>21.9</td>
<td>41.0</td>
<td>72.2</td>
<td>7.40</td>
<td>104.6</td>
<td>140.0</td>
</tr>
<tr>
<td>Hall</td>
<td>9.80</td>
<td>96.2</td>
<td>21.3</td>
<td>41.0</td>
<td>66.8</td>
<td>7.41</td>
<td>104.7</td>
<td>131.9</td>
</tr>
<tr>
<td>Montt 4.70 km, PB 429</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.7</td>
<td>78.0</td>
<td>17.1</td>
<td>26.9</td>
<td>68.9</td>
<td>7.45</td>
<td>107.3</td>
<td>138.7</td>
</tr>
<tr>
<td>Hall</td>
<td>11.6</td>
<td>83.2</td>
<td>16.7</td>
<td>28.0</td>
<td>68.8</td>
<td>7.52</td>
<td>105.7</td>
<td>136.0</td>
</tr>
<tr>
<td>Quilcha 5.34 km, PB 401</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>11.2</td>
<td>76.2</td>
<td>15.6</td>
<td>27.7</td>
<td>60.1</td>
<td>7.43</td>
<td>108.4</td>
<td>136.5</td>
</tr>
<tr>
<td>Hall</td>
<td>11.4</td>
<td>76.3</td>
<td>14.2</td>
<td>26.7</td>
<td>72.6</td>
<td>7.42</td>
<td>104.1</td>
<td>130.0</td>
</tr>
</tbody>
</table>
on December 14, 1937. That was the first break in the 10-member high-altitude circle. At the time we did not realize the significance of the fact that he had been a heavy cigarette smoker.

The Mississippi Study – 1939

In the spring of 1939 Greg came to the Fatigue Laboratory for control studies preparatory to a study in the humid heat of Mississippi. Sid Robinson who, after completing work for his Ph.D. at Harvard in 1938, had returned to Indiana, organized the study and transported a treadmill and other equipment from Bloomington to Benoit in Mississippi, his home state. Benoit is in the cotton belt about 20 miles north of Greenfield; Sid arranged to set up our laboratory in the gymnasium of the high school. Frank Consolazio took over Harold’s customary role in logistics; he loaded his car with chemicals and glassware and met Sid at Benoit. I arrived with others two days later to find the laboratory nearly ready. The party included John Gedgoud, a clinical investigator from the University of Chicago, Medical School, and from the Fatigue Laboratory, Will Forbes, John Wilson, Frank Consolazio, John Thompson and myself. Two Rockefeller fellows from Copenhagen completed the party: Erling Asmussen and Manus Nielsen.

Life was pleasant in Benoit, even though the maximum temperature averaged 34°C and the relative humidity at midday was about 60%. We found rooms in the homes of families who accommodated teachers during the school year. Greg and I shared a room in the home of Mrs. Fount Bisco, a charming and capable woman whose husband had seen better days; they had lost their plantation. She soon discovered our caloric requirement was about twice that of female school teachers so we worked out an equitable rate for meals.

The laboratory was soon functioning. Besides ourselves, we studied twenty-one young black sharecroppers and seven white sharecroppers. Acid-base balance, blood volume, water balance, work performance and sweat rate in outdoor walks were scheduled. Greg, Forbes and I were authors of a paper on plasma volumes (9). Contrary to earlier reports, we found an increase of normal range: 40.1 to 55.3 in Boston (mean 46.4), and from 45.6 to 52.9 in Mississippi. Their superior performance evidently depended on factors other than race, since two black house servants did not perform as well as some of us.

Greg and I had basal rates of oxygen consumption measured in ml/min that remained within the usual limits:

<table>
<thead>
<tr>
<th>Subject</th>
<th>Boston 1st week</th>
<th>Boston last week</th>
<th>Mississippi 1st week</th>
<th>Mississippi last week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dill</td>
<td>241</td>
<td>224</td>
<td>225</td>
<td>231</td>
</tr>
<tr>
<td>Hall</td>
<td>215</td>
<td>218</td>
<td>231</td>
<td></td>
</tr>
</tbody>
</table>

This was our first field study without Harold Edwards. But he and Johnson had taught Frank Consolazio many of the techniques used in the Fatigue Laboratory. Frank helped Forbes with studies of blood morphology and followed this up with Johnson after returning to Boston. They reported leucopenia is a normal characteristic of healthy young blacks when blood is taken in the morning with the subject resting (10). This was one of the first papers with Frank a joint author.

An illustrated account, which I wrote concerning that summer’s study, appeared in the Harvard Alumni Bulletin (4). In it I pointed out that “studies such as this have as their principal objective an extension of our knowledge of the physiology of man at work. By gradually selecting significant measurements, we have reached a stage where intelligible pictures are obtained from which one can discriminate between the physiological states of different individuals at work. We are convinced that, in order to be of maximum usefulness, attempts to picture and to interpret human societies should make use of the techniques of physiology and kindred sciences.”

Greg was a joint author with Wilson, Robinson and me of a report on properties of the blood of blacks and whites in relation to climate and season (18). We concluded that there was no clear evidence of dependence of the properties of arterial blood on climate or season. Blacks had a lower hemoglobin concentration than whites, but blood electrolytes were the same in the two groups. Here again Greg’s hemoglobin concentration was high and mine was low. Our arterial oxygen saturations were in the normal range:

<table>
<thead>
<tr>
<th>Subject</th>
<th>Total Hb g/100 ml</th>
<th>HbO₂ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dill</td>
<td>13.3</td>
<td>95.8</td>
</tr>
<tr>
<td>Hall</td>
<td>10.7</td>
<td>97.0</td>
</tr>
</tbody>
</table>

Table 2

PHYSICAL CHARACTERISTICS AND PLASMA VOLUMES

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age Yrs.</th>
<th>Ht. cm</th>
<th>Wt., kg Boston</th>
<th>Wt., kg Miss.</th>
<th>Plasma Vol., ml Boston</th>
<th>Plasma Vol., ml Miss.</th>
<th>Δ%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dill</td>
<td>48</td>
<td>179</td>
<td>79</td>
<td>77</td>
<td>3,750</td>
<td>3,570</td>
<td>–4</td>
</tr>
<tr>
<td>Hall</td>
<td>40</td>
<td>173</td>
<td>79</td>
<td>77</td>
<td>3,420</td>
<td>3,490</td>
<td>+2</td>
</tr>
<tr>
<td>Mean of 10 men</td>
<td>3b</td>
<td>1/b</td>
<td>/b</td>
<td>/3</td>
<td>3,440</td>
<td>3,580</td>
<td>+4</td>
</tr>
</tbody>
</table>
With support from the Federal Aviation Agency, six members of the high altitude party of 1935 visited the White Mountain Research Station in 1962 (6). Observations were made on respiration, acid-base balance and cardiovascular adjustments. Two or more days were spent at Crooked Creek (10,150 feet), at Barcroft (12,470 feet), and at the Summit (14,250 feet). Greg and Will Forbes each spent two additional weeks helping with the program. Figure 3 shows a group of us at the Barcroft laboratory.

Fig. 3. Greg with Bruce Dill and Ancel Keys at the Barcroft Laboratory, White Mountain Research Station, 1962.

Two graduate students, J. W. Terman and J. L. Newton of Indiana University, went as an advance party, set up the laboratory and remained until the end. Dill and Forbes arrived next, then Greg and MacFarland, and finally Keys and Talbott. Several of us were slower to acclimatize than 27 years before (10). The usual symptoms, dyspnea on exertion, headache, Cheyne-Stokes breathing at night and associated loss of sleep, were more evident and prolonged than in 1935. Greg did not complain, but he was quite uncomfortable at the Barcroft Laboratory. It seemed to us that his symptoms of mountain sickness were more severe than those experienced by the rest of us. He agreed to delay his visit to the Summit for a few days. By that time he was feeling much better, but as a medical precaution John Severinghaus spent the three days at the Summit with him. As it turned out, Greg felt quite well; it was John who experienced mountain sickness. Indicative of Greg’s attitude toward physiological research is the fact that he was the only one of our group to accept John Severinghaus’s invitation to submit to a spinal tap; John was making observations on regulation of respiration.

Our two graduate students obtained arterial blood for pH, pCO₂ and %HbO₂ on each subject at each station (39). Alveolar air was analyzed so it was possible to estimate the pressure head of oxygen from alveoli to arterial blood. One expects this pressure head to increase with age (11). The accompanying Table 3 compares findings on respiratory minute volume and on arterial pH, pCO₂, %HbO₂ and pressure gradient of O₂, lungs to blood. It is evident that Greg and I had much higher pressure gradients from lungs to blood than the young men. Our gradients in 1935 were as low as those of the two students. The increase in gradient may represent less adequate diffusion, or more likely poorly ventilated alveoli, due to increased residual volume. Greg and I had about the same percent of HbO₂ in arterial blood; this was attained by hyperventilation, more evident in him than in me. Values for arterial pH remained high during the entire period at altitude. The highest observed was on Greg when he first reached the Crooked Creek Station: 7.56; his %HbO₂ was 94. Hyperventilation was responsible; the associated arterial pCO₂ was 22 mm Hg. See Table 3.

The concentration of hemoglobin in blood during acclimatization did not increase as rapidly as in 1935. In fact, all but Keys

<table>
<thead>
<tr>
<th>Subject</th>
<th>Days at Altitude</th>
<th>VEBTPS liters/min</th>
<th>Arterial Blood</th>
<th>ΔpO₂ mm Hg*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>pH₅</td>
<td>pCO₂ mm Hg</td>
</tr>
<tr>
<td>DBD - 71 years</td>
<td>5</td>
<td>8.7</td>
<td>7.52</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>8.5</td>
<td>7.49</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>8.3</td>
<td>7.50</td>
<td>29</td>
</tr>
<tr>
<td>FGH - 66 years</td>
<td>3</td>
<td>12.0</td>
<td>7.56</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>11.6</td>
<td>7.52</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>12.9</td>
<td>7.50</td>
<td>27</td>
</tr>
<tr>
<td>JLN - 27 years</td>
<td>26</td>
<td>---</td>
<td>7.45</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>---</td>
<td>7.47</td>
<td>27</td>
</tr>
<tr>
<td>JWT - 23 years</td>
<td>26</td>
<td>---</td>
<td>7.47</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>39</td>
<td>---</td>
<td>7.51</td>
<td>25</td>
</tr>
</tbody>
</table>

* Pressure gradient between alveolar air and arterial blood.
showed a drop below control values at least once during the first days. My values were most exceptional, dropping for a week, then beginning to rise, and not reaching control values until after more than two weeks at altitude (17).

While Greg was most handicapped during the first days, he looked back on the experience with pleasure. He wrote me after his return, “I thought on the whole we had a pretty good summer at White Mountain. I really enjoyed it and I hope that you found the summer worthwhile. It was very good to see old friends again.”

Desert Reunion – 1964

Our plan for 1964 was to evaluate responses to desert heat and to compare them to our responses in 1932 or 1937. This was made possible by a grant to Indiana University by the National Institutes of Health. Talbott and the Consolazio brothers had been in the 1932 party; Greg and the Consolazios had been in the 1937 party (Figure 4). Our laboratory staff included Will van Beaumont from Indiana University, Earl Phillips from the University of Florida, and Don McGregor from the University of California, Santa Barbara. Figure 5 shows Greg analyzing blood, Boulder City, 1964.

![Fig. 5. Greg determining hemoglobin concentration at Boulder City, desert study of 1964.](image)

We had a laboratory and shower room at the Boulder City High School and did most of our walks around the high school quarter-mile track. Greg and Kenneth Hall came by car and brought equipment for plasma volume using $^{131}$I. Kenneth was a subject in walks around the track; other subjects were with us for a few days: Steve Horvath, Klaus Klausen from Copenhagen, and Knut Schmidt-Nielsen.

We took turns walking for an hour around the track at a fixed rate, either 80 or 100 m/min, using the techniques developed in 1937 for collecting and analyzing sweat and measuring its volume (13). It turned out that nearly all of us put out saltier sweat than when we were younger (14), though mine was still much saltier than Greg's. Kenneth was about the same age as Greg had been in 1937; his sweat was about as dilute as Greg's had been at the same age.

Greg was joint author of a paper in which we reported the relations between sweat rate, sweat composition, age, exercise and environment (15). Greg and Kenneth Hall also shared authorship of a paper on blood volume measurements in the desert and during a 10-day stay at Barcroft (14). This exploratory study suggested that during the first days at altitude hemoconcentration in young men reflects movement of water from blood to tissues while in old men there may be hemodilution with movement of water in the opposite direction. We are inclined to relate that difference to decline in adrenocortical activity. Salt concentration in sweat is used in clinical evaluation of adrenocortical function. In 1937 my sweat was saltiest and Greg's most dilute; in 1964 mine was saltier still and his was saltier than before. In 1962 my hemoglobin concentration dropped the most. These exploratory findings suggest that control of movement of water between blood and tissues in hypoxia and the saltiness of sweat both depend on level of adrenocortical function and its decline with age. More research is needed but, sad to say, Greg cannot take part.

At the end of the desert study, Greg drove to Santa Barbara; Kenneth had returned earlier to Durham by air. After Greg had been at Santa Barbara for some time, Kenneth flew out to accompany him on the return trip.

That summer money was short, so Greg and I shared a room in the Boulder City Inn and the others doubled up also. I became aware that Greg was in some pain during nights after his hour's walk. Kenneth and I discussed this with Greg; he agreed not to continue with the walks. After returning to Duke, he was examined by many experts, but they all finally accepted Eugene Stead's diagnosis that the pain related to reversible injury to ligamentous attachments of back muscles. Greg wrote in late September that he still had some pains after walking a mile or so.

Desert And Mountain – 1966

It was our aim in 1966 to measure blood volume and maximum capacity for supplying oxygen to tissues at Bloomington, at Boulder City, and at the White Mountain Research Station. Greg drove out alone; Loren Myhre, Douglas Brown and Kay Burrus came from Indiana University, Bloomington; and Gale Gehlsen, from Ball State University, Muncie, Indiana. The Dills had moved to Boulder City in May and were making plans to set up a desert research laboratory; money was promised the Desert Research Institute of the University of Nevada by the National Science Foundation effective July 1. That summer facilities at the Boulder City High School were used again. That summer's work on blood volume resulted in two papers with Greg as joint author. One described the use of $^{131}$I for measuring blood volume (32), and the other described blood volume changes during three weeks at high altitude (33). At Boulder City Greg's plasma
volume was within the normal range. His plasma volume in 1939 was 3420 ml at Boston, and 3490 in Mississippi (see Table 11). In 1964 at Boulder City, it was 3240, and in July, 1966, at Boulder City, it averaged 3630. Again in Boulder City, after the Barcroft experience and recuperation, it averaged 3580. Finally, in September, after return to Durham, it was 3390. It is remarkable that these observations from age 43 to 70 were within the limits, 3240 and 3580.

At Boulder City, Greg's hemoglobin concentration in blood was about 10% above mine as it had been ever since our measurements at the Harvard Fatigue Laboratory in 1934. We have made observations on others over a longer period, indicating that this is a persistent individual characteristic.

Greg and I both were somewhat apprehensive about his going to high altitude for three weeks. But he wanted to try it, so the six of us made the trip together. He had a bad first night, but he felt better the next day and was a subject in a blood volume measurement. He continued to be quite miserable, sleeping little at night. The fifth morning he went by helicopter to Bishop (about 4,000 feet altitude). Here he made a remarkable recovery, sleeping 14 hours the first night. After the second night, he announced his intention to try it again. But the old symptoms returned, and after the second miserable night, he agreed to leave for Santa Barbara. There Stephanie joined him. After an enjoyable week at Betty's home, they returned to Boulder City so Greg could help complete our studies. We waved farewell early one August morning as he and Stephanie left for Durham. We were not to see Greg again.

Greg's terminal illness was in the Duke Hospital where treatment measures were fruitless; he died on February 19, 1967. The final diagnosis was gradual failure of his heart. His ashes were held until spring, and then buried in the family plot at Milton.

Stephanie has written to me about the eloquent tributes paid at the memorial service, to his great achievements and his great humanity.

Epilog

I had an opportunity to review Greg's career at the Respiration session of the American Physiological Society at Chicago in April, 1967. After paying tribute to his record of 45 years, I spoke of his character, kindness, human understanding, great technical skill and his judgment of what constitutes a good experiment. I then recalled his enjoyment of life, his sense of humor and told one of his favorite stories, it brought down the house.

Two years later I was privileged to take part in the dedication of a magnificent memorial to Greg: The J. G. Hall laboratory for Environmental Research, at Duke University. There again I reviewed some of our experiences together and closed with the following verses paraphrased from sentimental verses he wrote celebrating my retirement in 1961.

WE REMEMBER HALL

On Andean cliffs our life was rough
All found sleeping very tough
But Sunday found us playing ball
That was where I first knew Hall

Singing "Mal Hombre," a Gaucho tune
Dining in a miner's saloon
Drawing blood from a llama's leg
That is how we remember Greg

Taking turns one by one
We walked a burro in the noontday sun
Through the mesquite and over the hill
Given water he drank his fill

On the hike to Santa Fe
With pemmican and ration K
Camping at night near a waterfall
There is where I remember Hall

During the War it was the task
To test performance of the oxygen mask
Some were baffled by facial convolutions
But Greg was quick to find solutions

The proper study of mankind is Man
Study him where'er you can
In heat or cold or dry or wet
Drawing blood or collecting sweat
In winter and spring, summer and fall
With great esteem we remember Hall.

In closing, a quotation from a burial service composed in 1920 by Percy Dawson, is appropriate. His career in physical education including a professorship at Duke, 1943-46, was interrupted by a pastorate in a Unitarian church. Percy died September 1970 at age 97; his burial service, as he requested, closed as follows:

"... all may see that even in his death his influence has not been in vain, but in dying as in living, he has served to advance through us the cause of truth and righteousness, of light and love. through the growing personalities of those near and dear to him."

ACKNOWLEDGEMENT

Invaluable assistance has been rendered by Greg's widow Stephanie, by his daughter Betty Bontwell, by his son Kenneth and by his sisters Marjorie Weber and Mary Christie. Several of his colleagues at Duke University helped me, especially Drs. Grey and Salzano. Useful details were found in the obituary published in the Physiologist (2).

References:

A NEW RESEARCH TRAVEL GRANT PROGRAM

A new program of research travel grants for medical scientists is being made available jointly by The Wellcome Trust in Great Britain and The Burroughs Wellcome Fund in the United States.

The program is so designed that a research worker engaged in a promising investigation in the United States can cross to Britain or Ireland to consult with or develop additional knowledge from research workers there, with a minimum of red tape and advance timing. The same arrangement is open to workers in Great Britain or Ireland to consult with research workers in the U.S.

In announcing the program, Lord Franks, Chairman of The Wellcome Trust, noted that “advances in the medical sciences might be hastened by workers being able to exchange information rapidly. The Wellcome Research Travel Grants provide a simple mechanism for research workers engaged in studies of an exceptional nature to come together for consultation and the expediting of their results, perhaps for publication and for the benefit of other workers in the particular field.”

The two private foundations have the knowledge to assess proposals from each one’s own country but decided that the joint arrangement would allow for fullest utilization of the expertise in each country to act upon proposals with good judgment.

The Wellcome Research Travel Grants may be applied for at any time during the academic year with the likelihood of a decision being given in a short period, thus allowing the workers to undertake their research abroad within several months of making application. Visits are expected to be of relatively short duration — two weeks to a maximum of three months. The research grants will take the form of a contribution towards the costs of travel and subsistence. The amount of the individual grant will vary, dependent on length of stay and location. No provision will be made for spouses or families.

Dr. Hitchings, President of The Burroughs Wellcome Fund, noted that “there exists a universal need for shorter term funding and a rapid means of making funds available to research workers with exciting leads that require collaboration with those in other countries. Government funding generally takes a year or more between the making of application and the receipt of money while other competitive one-time annual awards do not respond to the need. Our joint program will seek to fill the gap.”

The Wellcome Trust and The Burroughs Wellcome Fund each is setting aside $100,000 per year for three years for the Wellcome Research Travel Grants.

Inquiries originating in Britain and Ireland should be addressed to The Wellcome Trust, 1 Park Square West, London. Those originating in the United States should be addressed to The Burroughs Wellcome Fund, Research Triangle Park, North Carolina, 27709.

An Advisory Committee, composed of A. McGehee Harvey, M.D., as Consultant, Kenneth Brinkhous, M.D., and Paul L. Munson, Ph.D., of the University of North Carolina School of Medicine; and W. K. Joklik, D. Phil, and R. Wayne Rundles, M.D., of Duke University Medical Center, will assist the selection of U.S. recipients of the grants.
Leslie L. Bennett to Hy:

On July 1, 1977 I finally retired, a year later than I was supposed to have done so. I spent my last year in recall status as Vice-Chancellor Academic Affairs. All in all, I spent ten of the twelve years prior to July 1, 1977 in that position. I am very proud of the fact that for at least eight of those twelve years I managed to maintain some modicum of activity in research.

Since July 1, 1977, things have happened thick and fast. I have succeeded in breaking my ankle, having major surgery to remove three aneurysms (lower abdominal aorta and both common iliacs — no prior symptoms and an uneventful recovery); write another biographical sketch about Herbert Evans, write a short essay, the fate of which is undetermined, on Bennett’s Laws of Academic Life, and complete a special assignment for our Chancellor in the course of which I made two reasonably extensive trips across the USA to visit selected professional schools, hopefully to gain information to help us plan more sensibly for part of the future on this campus of the University of California. Amidst all this, Mrs. Bennett and I managed to spend eight days in Guadalajara.

As you see, my retirement has been moderately busy although there have been moments of boredom. At the moment I am debating among four options for the year 1978-79. A non-debatable event will be a month’s vacation in Europe in the early fall, a trip planned for 1977 but which had to be postponed. A major event this year will be my seventieth birthday at which time I plan on sharing with friends a bottle of 1908 vintage Port given to me two years ago.

Richard L. Riley to Hy Mayerson:

I continue to pursue my dual interests in respiratory physiology and airborne infection, but my base of operations is the type-writer rather than the laboratory. My last effort in physiology was a chapter for a book John West was editing, entitled “Development of the three compartment model for dealing with uneven distribution” of gas and blood in lungs. This was a look back at developments during the World War II years, with Joe Lilienthal, Fenn, Rahn and Otis, Scholander and Roughton, and others, including a little later, Andre Cournand.

My older brother, Edward C. Riley, and I have published an account of a measles epidemic in a school in which the index case probably infected 26 others, with whom she had no direct contact, by means of air recirculated through the ventilating system. There is reason to believe that most acute respiratory infections, the greatest causes of all causes of morbidity, are airborne, and recirculating air, as is now done in most new buildings, contributes to the problem. The recent outbreaks of Legionnaires’ Disease, attributed in all probability to air conditioning systems, is bringing this to public attention. Collaboration between microbiologists, engineers, epidemiologists, and renegades like myself who try to apply physiological principles to air conditioning systems, is not easy but it needs doing. The New York Academy of Science is sponsoring a conference on airborne infection in November 1979, that will provide a good platform.

I am ready for anything so long as it doesn’t move me from Petersham, Mass. The small town life suits me fine. My best to you and all members of the Committee.

Grayson P. McCouch to Hal Davis:

Some time back we sold our little farm and moved into a village of about 400 people over 65 years of age, called Crosslands, PA, within about four miles of our former home. Here Margaret finds an enthusiastic welcome for her flute among a variety of instrumentalists, and both of us find our time pleasantly occupied. What more could a man past 90 desire? Only that his brain be stocked with happy memories of such friends as you.

Fred W. Kasch to Bruce Dill:

I am continuing in my assignment at San Diego State University in teaching and operating the exercise laboratory and adult fitness program. Our studies have primarily been long term or longitudinal in nature (10-year study). I am free to move about, preferably to the Northwest (Wash., Ore.). The Adult Fitness Community Program is now in its 21st year (1958) and as a faculty program about the 25th year. It is self supporting, operating 12 mos. a year with approximately 115 persons. All four leaders are women. The laboratory personnel are about half men and half women, young people who are primarily students in training in exercise physiology, etc. Experimentation these days includes: hypertension, CHD, periodontics, migraine, life-style change, diet (low fat, Na, caffeine, sugar). Talks to hospital staffs on our work and long-range results have been rewarding as well as presentations to Dental Society, School administrators, podiatric and industrial recreation groups, C of C and Rotary clubs. The summer of 1979 takes me to Seattle, Walla Walla for workshop presentations as well as Irvine and Feather River, California.

Gustav Eckstein to Horace Davenport:

I am lucky. I am able to work at what seems not far from my pace half a lifetime ago. I keep at my “Pavlov”, which for obvious reasons is difficult and slow, and I am patchily at my autobiogaphy. It interests me every day to be at both books; both maintaining some connection to physiology; and that on myself, as great Sophocles already found, lets me “grow old learning new things.” What a satisfaction it is to look back over the road, see it absurd, occasionally wise, often annoying, enlarging in any case. About the writing: it is as difficult as it was in the beginning, the same old attractive fight. I do it, God knows, not for glory. From habit perhaps? I do not think it is that Anyway it is good for my body and for my mind. To look with some regularity at one’s survival, this also has a curious interest.

W. C. McNelly (Oxford, Ohio) to Edward Adolph:

Please accept my thanks for the congratulations for my eightieth birthday from the Committee. I get a letter each year from Bruce Dill asking for a note. I’ll get a note to him too. I remember riding from the APS meeting in Memphis (1937) to Cincinnati with Frank Hartman, Steve Horvath and you.

H. Stanley Bennett to Sid Robinson:

I retired as Chairman of the Department of Anatomy (Univ. of N.C.) in June 1977 and am continuing my activities in teaching and research as Sarah Graham Kenan Professor of Biological and Medical Sciences and as Professor of Anatomy. Surrendering administrative responsibilities for the Department has increased my time for research. I continue to do a considerable amount of editorial work for journals. Twice in my career I have had to drop out of active research completely. The first time was in World War II, when I served with the Marines in the South Pacific. The second time was when I was serving as Dean of the Medical School and of Biological Sciences at the University of Chicago. I found it slow to re-establish myself as an active scientist after the second lapse.
I have become interested in plant physiology, particularly in those aspects which closely parallel the physiology of animals. In collaboration with Professor Malcolm Brown of our Botany Department we have been exploring the generality of the occurrence of actin in plants and have addressed our thoughts and activities towards studies designed to give us better understanding of the role of actin and myosin in plant physiology. The recognition of the presence of actin and myosin in many non-muscle cells in animals and in a number of plant cells has led us to the view that it may be necessary to reformulate in general terms the physiological role of actin and myosin in cells.

Alerted by J. D. Pickstone's article in *The Physiologist*, Vol. 20, No. 3, June, 1977, on the ideas of the French physiologists, Magendie and Dutrochet, relating to absorption and osmosis, I found myself looking into the writings of Dutrochet and was impressed to note that in 1824 he expressed the view that plants and animals use the same physiological mechanisms. He suggested that the study of plants would, in many cases, lead to clarification of general physiological principles which would be applicable to animals as well. These predictions were brilliantly fulfilled in the genetic work of Mendel on plants, though it is seen now that Dutrochet was wrong in attempting to explain contractility on the basis of the vesicle theory and osmosis. It seems likely that he was right in postulating that plants and animals use the same mechanisms for motility. I hope that in the remaining years I can contribute to the development of this concept and anticipate that there will be challenges to which I would like to address myself for many years to come.

Best wishes to you all and especially to the Committee who encourage letters of this sort. Most of them are my warm friends and some were my teachers, to whom I owe much.

**Paul D. Altland** to Edward:

There has been no change in my research activities at NIH except that the pace is slower than in the past. I continue to study altitude tolerance in animals with emphasis upon enzyme changes. I have also been studying physiological, biochemical, and pathological changes in animals exposed to individual or multiple components of cigarette smoke. I have a post-Doc who is a great help in this work. I am also updating my contributions to the Biological Handbooks as well as the chapter on "Altitude and Exercise Effects on Animals" in the textbook *Progress in Biomechanology*. I plan to continue a while longer at NIH and reside in the Washington area after retirement.

**Wanda Wywricka** to Bruce:

I am continuing my experimental and theoretical work, and, to tell you the truth, I do not see any ending data for it. I am involved in two projects. One of them is a study of the imitations of the mother by weaning kittens in the development of food preferences. Our former experiments showed that adult cats would eat such unusual and inappropriate food for their species as bananas, cooked potatoes, or even tasteless and odorless jellied agar, when eating such food was rewarded by a desired hypotonic stimulus. When 6-8 week-old kittens accompanied their mother-cat during the session, most of them imitated her in eating the unusual food. After weaning, and in the absence of the mother, most of these kittens continued to eat that unusual food whenever offered, in the presence of meat pellets. Parts of this study are already published.

Another project is a study of central neural influences on gastric acid secretion in cats. This is part of a program of the Center for Ulcer Research and Education (CURE); I am one of its "key investigators." Our experiments showed that electrical stimulation of the hypothalamic sites where stimulus-bound feeding was obtained in satiated cats, did not produce any significant increase in acid secretion in these cats when hungry. However, similar stimulation in other, non-feeding sites in the anterior-preoptic hypothalamic zone did produce an increase in acid secretion. On the other hand, bilateral lesions in the lateral hypothalamus which had resulted in aphagia, or lesions in the ventromedial hypothalamus which had resulted in hyperphagia, also produced some changes in gastric acid secretion; these changes, however, were not correlated with the changes in food intake produced by these lesions. All these data suggest that the hypothalamic structures related to gastric acid secretion are not identical with structures related to eating. Some of these results are already published.

I have decided to discontinue my work related to CURE and to retire in December. However, I will continue my research on the development of independent feeding and food preferences. I also plan to join a program on the neurobehavioral aspects of alcoholism, organized by the Brain Research Institute and Neuropsychiatric Institute at UCLA. I feel that it is too early for me to retire. I am permanently engaged in writing articles on my current results. I would be happy to be a consultant or an advisor for the problems related to conditioning or the neurobehavioral mechanisms of feeding, to give a few lectures or seminars on these problems. I like to travel, but would rather not move to another area for a permanent stay.

**Milton Mendelowitz** to Edward:

I am including a recently completed Curriculum Vitae. I am still practicing medicine and working half time in research with special emphasis on hypertension theory. The latest paper presents a new concept of the genetic defect in human essential hypertension. I take longer vacations, although during one of this year's holidays, I visited Morocco and sat in on the Fifth Meeting of the International Society of Hypertension in Paris. I also do some sailing, with my wife as crew, and enjoy this very much. It would take a very challenging offer to move me from my present activities, but I am always available for consultative and advisory demands. [The Mendelowitz bibliography included 318 journal papers and four books. He is Price Professor of Medicine Emeritus at Mount Sinai Sch. Med.-ED.]

**Arthur W. Martin** to Hal:

The level of devoted service the APS has always gotten from its officers never ceases to amaze me and the activities of your Committee now serve as a reminder. I do not retire until age 70 and so I still have interesting classes to teach, a reasonably equipped laboratory, and an effective aquarium. I am finally beginning to understand my research materials: cephalopods, spiders and worms. I spent a month in Newfoundland between the teaching of Summer School and Autumn Quarter and made considerable progress in understanding the differences in excretory physiology between squids and octopuses.

I have been amused, and put to considerable personal expense, by a mistake in judgment I made nearly fifteen years ago. I had had fine support from the NIH through the Heart Institute. Then I put in a couple of years as a Program Director at NSF, and when I returned to teaching felt it more proper to let my NIH support lapse and get research support from NSF. I knew, of course, of the substantial loyalty with which the Heart Institute supported its investigators, and I regret not having stayed with it. Although I am still publishing, my work is out of the mainstream of modern physiology and the NSF has decided not to support it. I believe the NIH would have seen me through to retirement and so I call this to the attention of the younger generation as per-
haps worthy of note and, when one stops to think about it, what a wonderful thing to say about an organization like NIH. After all I had years of substantial support, and there are strong pressures to support young men who are trying to get established. I am willing neither to quit work nor to stop writing and have three active programs in progress. Needless to say I am not looking for work elsewhere.

Willard M. Allen to Hal:

I continue to enjoy my post as Associate Dean in charge of admission at the University of Maryland School of Medicine. We have survived the Bakke Case, compiled with the Public Law forcing us to accept transfers of United States citizens from foreign medical schools, and are now informed that we must not reject applicants on the basis of age or handicap. The big push now from the politicians emphasizes maldistribution. We are expected to correct that. I remain optimistic. There is one bright light on the horizon. The young people who are foolhardy enough to apply have superb intellects, an unwarranted faith in the future, and high ideals. Most of them will become good physicians too.

My teaching is rather limited. I give an occasional talk on the female sex hormones and office gynecology to physicians attending our courses in continuing education. Now and then I am invited to tell the story of progesterone. I seize these opportunities with zeal as they give me the opportunity to blow my personal horn rather effectively. Not many of the modern-day zealots know that the discoverers of progesterone, all three of us, are still above ground. Dottie and I relish each sunrise as much as ever.

H. Roberta Hafkesbring to Dr. Prosser:

In June 1964, I retired as Professor of Physiology at Woman's Medical College (now the Medical College of Pennsylvania) and left immediately for Korea. I served a year as Visiting Professor (teaching) two full sessions in the Medical College of EWHAn Woman's University in Seoul. I fell in love with the country and its people, and returned in 1966, 1967, 1968, and 1971, each time on a full time basis. After my 4th or 5th "so called retirement" I moved to a lovely retirement home in Claremont, California. Enjoying excellent health, I have had several extended trips, including "round the world" and three weeks in Africa. My life here is very pleasant and interesting and there is time to really read a wide variety of books.

A. Baird Hastings to Dr. Prosser:

I am still unretired and unrepentant. I manage a four-hour afternoon in my office at the Physiological Research Lab. This marks the eleventh year I have been in residence at Scripps Institution of Oceanography with the title of Research Associate in Neurosciences, UCSD Medical School. I enjoy my association with Fred White, the successor to Pete Scholander who is still around, titillating us with his unorthodox ideas. There are also a number of young men, students and post-docs, who teach me more than I teach them. My one regret is, that I waited so long to realize that life in the "sea-with-out us" is of equal interest with the "sea within-us."

WORKSHOP ON IMPLANTABLE TRANSDUCERS AND SYSTEMS: PACKAGING METHODS AND TESTING CRITERIA

The Workshop will be held at Stanford University on June 27-29, 1979. The subject of the Workshop has been chosen to bring together those researchers, fabricators and users of biomedical implantable electronic transducers and systems who are concerned with the long-term reliability of such systems. The Workshop is concerned with such topics as encapsulation materials, current practice, accelerated testing techniques, research into new solutions, acceptable failure rates and in-vivo system calibration. A digest will be prepared of all papers presented at the Workshop and will be available for distribution at the Workshop. In order to encourage participation in the discussions, attendance will be limited to 150 participants. Further information can be obtained from:

Professor James B. Angel
Dept. of Electrical Engineering
Stanford University
Stanford, CA 94305

Xth CONGRESS OF THE INTERNATIONAL ACADEMY OF LEGAL MEDICINE AND SOCIAL MEDICINE

The Congress will be held in Lyon, France, August 27-30, 1979. Six topics have been chosen: Thanatology; Catastrophe and Collective Death; Former Condition and Compensation for Bodily Injury in Common Law; Organization of a Medico-Legal Service in the Hospital; Professional Discretion and Insurances; and Oppression of the Human Body.

FIRST INTERNATIONAL CONGRESS OF NEUROTOXICOLOGY

Promoted by the Italian Society of Toxicology, University of Pavia, the Congress will be held Pavia-Varese, Italy, September 27-30, 1979. The Symposium will consist of invited lectures and communications.

For information regarding both Congresses contact: Professeur Louis Roche, Faculte de Medicine Alexis Carrel, Rue Guillaume Paradis, 69008 Lyon, France.
This assessment of the state-of-the-art with regard to physiological simulation would be incomplete without a clear statement of the importance of conventional physiology laboratory exercises involving living material. Today, many medical schools are decreasing the number of hours of required laboratory work associated with their medical and graduate student physiology courses. Many reasons are offered for this change: a) many students have already performed classical physiology experiments prior to entering medical school, b) curricular reorganization has encroached on the time available, c) successful laboratory teaching must be done in small groups and thus requires an extensive commitment of faculty time, d) equipment for such teaching has become increasingly sophisticated and therefore expensive, e) the cost of laboratory animals, especially the larger mammals, has become prohibitive at a time when medical schools are facing severe pressures for cost containment, and f) recent federal regulations with regard to human experimentation place new burdens on those who would use students as experimental subjects. All these reasons have some measure of validity, but my purpose is not to catalog constraints. Rather, I desire to restate the case for physiology laboratory exercises and thus help us to resist those forces which cause us to reduce our commitment to effective laboratory teaching.

An Opportunity to Discuss the Ethics of Medical Research

As practitioners of the basic medical sciences we have a responsibility to foster the professionalization of young people who come to us for advanced training. One of the societal misconceptions supported by media dramatizations is that scientists are dispassionate and that their desire to obtain knowledge provides them with a rationalization to exceed the bounds of propriety with regard to the treatment of experimental animals. The best way to combat these erroneous views is for us to offer laboratory exercises in which we behave as exemplary humanitarians as we handle experimental animals and living tissue derived from them. This is particularly important as it pertains to anesthetizing large animals. Too often that crucial activity is left in the hands of those who are not well-trained and who have little sense for the reverence of life. Thus, if a dog or cat is delivered to the teaching laboratory so lightly anesthetized that the animal re-enters the excitement stage, a very poor impression is made on students who do not yet appreciate that reflex movements and cries do not originate from a conscious level. Similarly, an animal that has received too much anesthetic must immediately be placed on a respirator which creates a mechanical substitute for a physiologic process and is a less than ideal situation.

The professionalization of the student involves an understanding of what can best be learned from lectures and textbooks and what requires exposure to the living material. The justification for the use of animals in drug testing and other forms of medical research should be developed. Yes, we can use computer support to undertake some of this teaching, but I do not believe the simulations will carry as much impact with regard to the ethics of medical research as the presence of a live animal in an appropriately designed laboratory exercise where the faculty demonstrate a high degree of awareness for humanitarian considerations.

An Opportunity to Observe the Unique Characteristics of Living Material

Just as every human being is unique, that principle applies to lower forms of life: no two animals will behave in exactly the same manner. Though possible through creative programming, it is more difficult to create uniqueness in a simulation than it is to reach into the living world where it is a given. Students of the health professions tend to think of experimental animals as patients and will have a genuine sense of loss if the animal succumbs before the laboratory is completed. The fragile thread of life can be broken without much warning, especially for those who are not yet trained in reading signs of decompensation. Equally important lessons are available while the animal still lives: the presence of a blood supply and resilient tissues which have not been hardened or discolorated by the embalming process; the redundancy of physiological mechanisms where several processes carry on the same function to assure its proper performance; the amount of abuse that living material can absorb before reaching an irreversible state; the relationship between
stimulus and response and those limits where a further small in
crease in stimulus brings about an entirely different response.
Since life is the stuff with which the student eventually must
deal, there is no substitute for providing supervised experiences
where this learning can take place effectively.

An Opportunity to Deal with Biological Variation

In an earlier era, much of the biostatistics relevant to the prac-
tice of medicine could be derived from the techniques used to
treat biological data emanating from physiology laboratory ex-
cercises. Today we have special courses in statistics which approach
the subject from a theoretical point of view and are more likely to
deal with population parameters rather than individual variation.
Yet each person who is to be responsible for prescribing medica-
tion, and we have today treatment modalities much more power-
ful than those of an earlier time, must ultimately develop a sense
of posology. To me, it is better to develop this skill on an
anesthetized animal than to have to learn it at the expense of the
first few patients that a new physician begins to treat.

Similarly, having attempted to perform chemical analyses on
blood and urine in the physiology laboratory creates a proper
degree of skepticism in the would-be physician with regard to the
validity of clinical laboratory data. As miniaturization and automa-
tion alter the clinical laboratory, an aura of mystery shrouds how
it is possible to obtain so much information from such a small
sample. The fundamentals of sampling technique are often ig-
nored and failure to protect specimens as they are transported
from patient to laboratory exact a toll of misinformation. Some of
these obligate sources of error seem to recede when the final
results are presented in an authoritative format which clearly
shows the validity of the analysis as compared with interspersed
standards.

An Opportunity to Expose the Student to Medical Procedures

We should not omit from this discussion those physiology ex-
cercises in which a student is used as the experimental subject.
Here is an important setting for the embryo physician to voice
concerns which any patient might have when first exposed to
electronic monitoring or other recording procedures. How often
will students make inappropriate jests about electrocution at the
expense of the subject who has been fitted with electrodes for
electrocardiography? When a student has been subjected to the
discomfort of an insufficiently deflated sphygmomanometer cuff
will he be more careful when it is her/his turn to make a blood
pressure measurement.

Much of the practice of medicine deals with specimens derived
from blood, urine, feces and other body fluids. When the latter
must be obtained at some discomfort to the patient, it is instruc-
tive for the physicians of tomorrow to be familiar with these pro-
cedures as a result of personal experience. This is not to suggest
that swallowing a gastric tube should be required in the absence
of a person who can assist the student in avoiding a vomiting
response. The important point is that exposure to medical pro-
cedures and the development of professional attitudes regarding
how to handle patient anxiety, how to perform simple clinical
measurements, and how to collect, store, and analyze specimens
derived from humans are all worthwhile by-products of the
physiology teaching laboratory.

Finally, it should be recalled that physiology, an amalgamation
of physics and biology, is a science deeply rooted in the ex-
perimental method. To teach physiology as a description of facts,
without providing each student a personal context of the
methods used to develop this body of knowledge, is at best to
rob it of its vitality; at worst, such teaching is a travesty on those
whose learning has been intrusted to our care.

THE INTEGRATED FUNCTIONAL LABORATORY AT
THE UNIVERSITY OF TEXAS MEDICAL BRANCH
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The multidisciplinary laboratory (MDL) which was introduced
at Western Reserve University (1,2) has received widespread ac-
cceptance largely because of the saving in laboratory floor space,
and to some extent equipment, which it achieves. As originally
proposed, the MDL replaced individual department laboratories
with one facility where students conducted laboratory exercises
required for each course. Each institution which has elected to
adopt the MDL laboratory has modified the basic concept to con-
tain to institutional considerations (3-6). The interdepartmental
facility at the University of Texas Medical Branch differs from
those of other institutions so extensively that it is not longer iden-
tified as a MDL and has been given the name Integrated Func-
tional Laboratory (IFL). Most of these differences are either direct
or indirect consequences of a central concept: that the laboratory
should integrate the material introduced in the various disciplines
rather than be a place where the student may study each
discipline serially with no attempt at intercorrelation.

Organization

The class, consisting of about 220 students is divided into two
sections which meet for laboratory on different afternoons of the
week. The sections are further divided into 24 teams each. As a
rule, four teams conduct the same experiment on each laboratory
day however, there is nothing to prevent combining or further
dividing teams if necessary for the conduct of the experiment.

On the time scale, the course is also divided into two portions.
Students take the first half of the course (12 weeks) in their sixth
month of medical school. The second half is taken six months
later. The laboratory for three other courses, microbiology,
pathology and histology utilize the IFL facilities when they would
otherwise be idle. The first half of the IFL course runs concurrent-
ly with the physiology, neuroscience and cell biology courses.
The IFL experiments, therefore, are designed to reinforce the
material presented in these courses. The second half of the
course emphasizes pharmacological principles for similar reasons.

While the conduct of each experiment differs depending upon
the topic, technical and instrumentation problems, and to some
extent, the preferences of the instructor, in every case a primary
objective is to encourage student-to-faculty exchange. This is dif-
ficult to achieve in some laboratories because the experiment
demands the student’s entire attention or because of equipment
noise. Therefore most experiments incorporate a conference
period where misconceptions and weak points are sought out
and corrected.

Personnel

The operation of the laboratory demands that the preparations
for 24 teams be completed by one o’clock each laboratory day.
This entails a great deal of manpower but only for two days per
week. The hiring of technically competent full-time personnel to
meet these requirements is avoided by retaining registered nurses
and graduate students who, because of outside commitments,
find the two-day week more satisfactory than full-time employ-
ment.

In addition to the part-time staff there is a permanent staff con-
sisting of a director and assistant director (both of whom have
faculty appointments) a supervisor, secretary and technician. A
Laboratory Experiences

During each week of the course every student is expected to participate in one laboratory and its associated conference. The conference may follow the lab immediately, or the following day. Or, it may be combined with the laboratory and, in one case, it precedes the laboratory. During the conference the experiment and results are discussed. Attempts are made to correlate the discussion with material presented in other courses and, where possible, clinical significance is emphasized.

**Advantages**

The primary advantage of the IFL is that it pulls together facts from various disciplines which, prior to the inception of the IFL, were often presented independently by lecturers in various departments with no attempt at correlation. It also benefits the student by providing him with a repetition of material which he may not have absorbed from lecture. Since many of the laboratories are conducted several months after the pertinent lectures, it also provides a “refresher” function in some instances.

Physiological, biochemical and pharmacological topics have been combined in the make-up of the majority of experiments. To date, attempts to incorporate pathological and microbiological topics have been less successful. In only two experiments, one dealing with hepatic necrosis secondary to biliary obstruction and the endotoxic shock experiment are pathological aspects emphasized. And, in spite of what appears to be a natural affinity between anatomy and physiology, it has not been possible to develop meaningful experiments in which the anatomy of the subject was a major consideration. Consequently, anatomy, pathology and microbiology laboratories remain under departmental auspices although, several departments share facilities with the IFL.

**TERM II EXPERIMENTS**

- The Intracellular Action Potential
- Spinal Cord Reflexes
- Erythrocyte Glucose-6 Phosphate Dehydrogenase (G6PD Deficiency)
- Hepatic Necrosis and Billiary Obstruction
- Studies of the Contractile State of the Myocardium in the Intact Dog
- Events of the Cardiac Cycle
- Secretion and Absorption
- Hemorrhagic Shock
- Human Pulmonary Function
- Acid Base Balance
- Tumor Cell Kinetics
- Inborn Errors of Metabolism

**TERM IV EXPERIMENTS**

- Temperature Regulation
- The Effect of Drugs on Respiration
- Effects of Exercise on Cardiovascular Function
- Endotoxic Shock
- Immunology
- Glucose Tolerance Test
- Renal Drugs
- Anesthesiology
- Effects of Drugs on Cardiovascular Reflexes
- Neuromuscular Transmission
- Uterine Responsiveness to Hormonal Influences
- Renal Excretion of Salicylates

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The veins are more than conduits for the return of blood. In this presentation, I plan to give perspective, some of what is known, and place major emphasis on pitfalls of understanding and interpreting venous physiology. First of all, what do we know for sure? The veins are compliant, such that an increase in internal pressure causes an increase in volume. They have smooth muscle, tor, when stimulated, they contract and thereby reduce the contained volume at the same pressure. But, they are innervated sparsely. We also know much about the elastic nature of the large veins (>2 mm in diameter) and quite a bit about the pharmacology of the veins that can be easily visualized. What we do not know for sure is the importance of the veins in the reflex control of cardiovascular function. How much do they influence arterial pressure and/or cardiac output and under what conditions? Many of us think they are important, but many others disagree. The effect is clearly relatively small, but may well be both fast and significant.

The literature concerning the capacitance vessels is much smaller than that of the arteries and resistance vessels. Yet, my files contain over 500 papers, and I am confident that there are at least 1000 significant papers. An almost exhaustive and a superb starting place to learn about venous physiology is Shepherd and Vanhoutte’s book, *Veins and Their Control*, published in 1975 (17).

The Pharmacology of Venular Smooth Muscle, by Burt Altura (2), appeared very recently and reveals an extremely diverse and complex system. It is based heavily upon Altura’s own direct observations of the microvasculature. It seems rather clear that there is a high degree of heterogeneity in the response of the venules to vasoactive agents. Even though the very small venules have very little smooth muscle, pericytes may respond to vasoactive agents because these venules (under some conditions) become smaller on stimulation. Muscular venules (30-100 μm in diameter) are without sympathetic innervation or are sparsely innervated. This is in great contrast, of course, to the innervation of the arterioles. Small veins (0.1 to 0.3 mm diameter), on the other hand, have both muscle and innervation. The peripheral veins (0.2 to 2.4 mm diameter), as you will recall, contain the largest fraction (60%) of the total blood volume. Although this volume is large, we do not know how much is available for redistribution. Catecholamines – especially epinephrine – cause the capacity vessels to constrict. The pattern, however, is complex being related to dose and varying from tissue to tissue. Histamine and bradykinin tend to cause relaxation of the venules. If there is relaxation, it would then appear that there must be some tone, but we do not know for sure if there is any or what causes it. We also do not know for sure that there is any myogenic response of the veins, even though this would be important to the human on standing.

A question Altura discusses (as have many others before) is whether the receptors for the capacity vessels differ from those of the arterioles. We know, for example, that the spleen responds dramatically to catecholamines and to sympathetic stimulation. The arterioles, of course, constrict in response to norepinephrine, but low concentrations of epinephrine will tend to cause dilation. In a recent study (10) of the intestine of dog perfused at constant flow, we found that isoproterenol infusions caused much dilation of the resistance vessels, but little change in contained volume. What of the capacity vessels of the liver, for example? Are they innervated? To what hormones do the capacity vessels of the hepatic vasculature respond? A final point to be gleaned from Altura’s review, which should be obvious to all of us interested in cardiovascular physiology, is that anesthesia, age, sex, electrolyte concentration, species, all can cause significant differences in vessel responsiveness. More research is needed.

Potential Importance Of Venoconstriction

Just what is the importance of the capacity vessels in cardiovascular function? We know that filling of the heart determines cardiac output. Obviously, cardiac contractility, heart rate and pressure load and important, too, but without filling, there is no cardiac output. In addition, filling of the right heart is determined by the right heart compliance, the resistance to venous return and the pressure gradient from the capacity vessels to the right heart. The filling pressure of the capacity vessels, in turn, is determined by blood volume and vascular capacitance. This relationship between cardiac output and venous return was in large measure developed, clarified and brought to our attention by Arthur Guyton. The “Guytonian relationship” is on a par with Starling’s Law of the Heart, in my opinion, as a conceptual framework for our understanding. Do you remember Guyton’s Physiological review paper (7) of 1956? The equilibrium point (operating point, A) of right atrial pressure (Fig. 1) determines, on the one hand, the cardiac output — given the state of the heart and the pressure load — and, on the other hand, it determines the venous return. Now, if the mean circulatory filling pressure (MCFP) is increased by venoconstriction or increased blood volume, the operating point equilibrium then occurs at a higher cardiac output (C).

![Diagram](image-url)

Fig. 1. Determination of cardiac output by equating venous return curves with cardiac response curves. Redrawn from A.C. Guyton, *Physiol. Rev. 36*:123, 1956, Fig. 6.

If we look at the relationship between the systemic pressure load and the right atrial pressure in another way, we have the classic presentation (Fig. 2) developed by Herndon and Sagawa (10). With reflexes blocked, note the extreme steepness of the effect of right atrial pressure on left ventricular output (systemic flow). Because
the systemic arterial pressure is developed by the left heart, the right heart is buffered from the systemic pressure load, and so until the systemic arterial pressure becomes much higher than normal, the right heart output is independent of the systemic arterial pressure. Note that if reflex activity is held constant, then there is nearly a 50% change in cardiac output with only a 1 mmHg change in mean right atrial pressure. Thus, cardiac filling pressure is exceedingly important. This pressure, in turn, is determined by the capacity vessel activity and the blood volume. Thus, the status of the venous wall tone is of great potential importance.

**Venous Pressure-Volume Relationship**

The pressure-volume relationship of the small veins is not well known. Figure 3, from one of Robert Alexander’s early papers (1), is a depiction of the various pressure, on the vertical axis, and total venous volume, on the horizontal axis. Note the marked changes in the proposed pressure-volume relationship, as were deduced from the techniques available at that time. At the left, the constricted vessels were theorized to have a large change in pressure with a small change in volume, and thus were much stiffer than when dilated (at the right). Is this the true situation? What is the normal pressure range? Is it only at the lower part of the figure? At the higher (physiological?) pressures, the constricted vessels are more compliant than the dilated vessels. Since 1954, techniques have become available to provide more information.

In Figure 4, a more recent depiction of the pressure-volume relationship is presented. An important point I would like to emphasize is the relationship between compliance ($\Delta V/\Delta P$) of the capacity vessels and the unstressed volume. The heavy line (A) depicts the pressure-volume relationship that seems reasonable for these vessels. If we extrapolate the somewhat linear portion to zero pressure, we have what is called the unstressed volume, $V_u$. As the contained volume becomes less and less, these vessels are no longer distended, and the volume contained in them in the relaxed state is removed with little change in pressure. Although this relationship is reasonable for an isolated vessel, it is probably not valid within the mass of tissue, for as the non-distended volume is removed, a negative pressure is probably required to remove the remaining volume. Please note that an active capacity vessel change can occur — that is, active in the sense of smooth muscle contraction — to cause a displacement of blood ($\Delta V$) for increased cardiac filling at the same transmural pressure of the small vein by either a change in compliance (line C) from the same unstressed volume (and the curve becomes more and more vertical) or there can be a change in unstressed volume (line B) with the curve being moved toward the zero volume axis, with no change in compliance. As some of our data would suggest (15), both mechanisms operate. It is not enough just to measure compliance or filling pressure or volume to evaluate the degree of activity of the capacity vessel smooth muscle. We cannot get an unequivocal answer to the status of changes in the capacity vessels by measuring compliance only; unstressed volume is also needed. Thus, the actual contained volume and the transmural pressure must be estimated. Isotope loading or indicator dilution techniques seem to be the only reasonable approach to estimating the total contained volume of the vasculature within the mass of a tissue. With a nonlinear situation such as this, life is not easy for the investigator!

**Effect Of Flow On Small Vein Volume**

A second important concept is that passive changes in capacity vessel volume can occur — and thereby change volume, and thereby redistribute volume from the periphery to the heart, thereby to increase filling and cardiac output — merely by a change in blood flow. The logic for this is presented in Figure 5. On the left are depicted the arterioles and blood inflow; in the middle, the capillaries and venules; the capacity vessels or small veins are toward the right, with blood exiting the veins at the far right. The flow through this system is due to the pressure gradient from the arterioles to the capillaries, divided by the resistance, and must also itself have no net fluid exchange to be equal to the pressure gradient from the capillaries all the way out to the largest veins divided by the resistance (Rv). If we have an increase in resistance into the

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**Fig. 2.** Interaction of right atrial filling pressure and mean arterial pressure on cardiac output. From Selkurt: Physiology, Little Brown, 1976, Fig. 15-7; redrawn from Herndon and Sagawa, Am. J. Physiol. 217:65, 1969.

**Fig. 3.** Venous distensibility patterns. Redrawn from R.S. Alexander: Cir. Res. 2:405, 1954, Fig. 1.

**Fig. 4.** Active capacity vessel changes by either changes in compliance or unstressed volume.
capillaries from the arterioles — arteriolar vasoconstriction (increased Ra) — this will decrease flow, if arterial pressure is maintained constant and capillary pressure does not change appreciably. (The capillary pressure will, of course, decrease some.) This decrease in flow necessarily will decrease the pressure gradient from the capillaries through to the veins. This decrease in gradient occurs inevitably with a decrease in flow, although capillary and venous pressure can change somewhat. As a consequence of the decrease in pressure drop across this system, there will be a decrease in average pressure within the small veins (Psm). The decrease in internal pressure will thus inevitably cause a passive decrease in volume, if we assume that compliance is constant. Thus, a mere decrease in flow will cause a passive decrease in venous volume, and so it is not enough just to measure changes in capacity vessel volume to assess active venuconstriction. If we are to evaluate reflex control of these beds, we must also maintain the flow constant through them, or have enough measurements to be able to assess changes in the pressure-volume relationship.

\[
\frac{P_a - P_c}{R_a} = \text{Flow} = \frac{P_c - P_v}{R_v}
\]

If: \( R_a \downarrow \rightarrow \text{Flow} \downarrow \rightarrow (P_c - P_v) \downarrow \rightarrow \left( \frac{P_c - P_v}{2} \right) \downarrow \rightarrow P_{sm}
\]

If: \( C = \frac{A V}{A P} - k \) Then: \( P_{sm} \rightarrow P_{trans} \rightarrow |\text{Volume}|

In summary, the cardiovascular reflex that influences the resistance vessels and thereby changes blood flow will passively cause a change in contained volume, without necessarily having influenced the activity of the smooth muscle of the capacity vessels. This effect is large. In a recent study (16), we (as well as others) have provided numbers for this volume change versus flow relationship (Fig. 6). By vasoconstriction that would reduce flow to near zero, nearly 40 ml of blood per kg of tissue will be lost from the gut (from a contained volume of 105 ml/kg to 65 ml/kg). Even more important, if venous pressure is also decreased, there will be still more volume lost. In addition, if the smooth muscle of the capacity vessels is activated, it would appear that yet more can be removed, but the role of reflexes is not, at this stage, fully known.

**Reflex Control Of The Veins**

Otto Gauer, a giant among physiologists and a leader in the studies of plasma volume control, in Vol. 9 of *International Review of Physiology* (5), concluded that "reflex control of volume, rather than an increase in venous tone" is required "to regain the normal filling state of the circulation" following small hemorrhage. It seems clear that he considers that under situations of light stress, venuconstriction is minor. In a review in 1970 (6), he concluded (with the help of the data presented in Fig. 7) that there was little or no change in capacity vessel tone in response to a hemorrhage of up to at least 10% of the blood volume. Although there is no question that blood volume control, in the long run, is more powerful and has a wider range of possible activity than venous tone control — indeed, it is essential to attain a fully normal filling state of the circulation — I submit that Gauer's conclusions are based on inadequate data, and that the capacity vessels change in a nearly linear manner in response to hemorrhage or transfusion (4) — but then, people are not dogs. A valuable analogy can be drawn between the relationship of venous tone and blood volume as they influence venous return and the relationship between pulmonary control of blood pH as related to renal control of acid-base balance. Only the kidneys can ultimately provide a restoration of total acid-base balance, but the respiratory-bicarbonate system is both fast and extremely important under short-term conditions whereby pH must be held at physiological levels. The active changes in the venous system may also be of importance in rapid, short-term compensation for small hemorrhage or in response to postural changes in men. The data, however, are not all in and the controversy continues.

![Fig. 5. Passive change in capacity vessel volume from changes in flow.](image)

![Fig. 6. Effect of blood flow on vascular volume. From Rothe, Johns and Bennett. Am. J. Physiol. 234:H7, 1978, Fig. 3.](image)
Another important finding of the Shoukas and Sagawa study (18) is that the compliance did not change appreciably in response to the changes in the carotid sinus pressures. They thus concluded that the change in the capacity vessel pressure-volume relationship was in terms of the unstressed volume. To repeat a previous conclusion, vascular compliance does not provide a total measure of the status of the capacity vessels.

In a recent monograph on peripheral circulation (11), Paul Johnson estimated that denervation would cause the blood volume of tissue to increase about 20%, and with maximal stimulation, he felt that one could expect a 30% decrease in contained volume. Although reasonable, no reference was given for the data to support these conclusions and so more research is needed.

In an attempt to assess the range of possible control of the pressure-volume relationship of the vasculature of the dog, we compared control pressure-volume changes 5 minutes after a volume change to results in which we had attempted to constrict the capacity vessels maximally with norepinephrine or block all activity with hexamethonium (4). From these data (Fig. 9), we concluded that the maximum range of smooth muscle control was of the order of 15 ml/kg body weight at a mean circulatory filling pressure of about 10 mmHg. The effect of ganglionic blockade is shown in Fig. 10 (bottom). It would appear, then, that the veins may have a larger potential range than is activated by the arterial pressor receptor system. Differences in the physiological state of the animal, especially as related to anesthesia, could be important.
The movement of water across the capillary, as capillary pressure is changed, is another complication in the assessment of the vascular pressure-volume relationship at the microvessel level. In our study (4) of the total vasculature, we hemorrhaged or transfused the animal over a period of about 20 seconds and then determined the mean circulatory filling pressure (MCFP) at 30 seconds. We repeated the MCFP determinations at 2 and 6 minutes, and, as can be seen in Figure 10 (top) the relationship changes with time. With the repeated determination of MCFP after a transfusion, the MCFP was found to decrease significantly. On the other hand, following hemorrhage of large volumes, the MCFP returned back toward normal. This suggests a compensatory mechanism. Part of this was due to reflex activity, but another part was certainly due to fluid shifts across the capillaries.

As Arthur Guyton pointed out years ago (and a point to keep in mind concerning the capacity vessels), the smooth muscles of the veins are slow in responding to stimulation. Even though the information from receptors to brain and out via the sympathetic nerves to the periphery may be transmitted in less than one second, there seems to be very little change in the capacity vessels before at least 5, and probably to 10, seconds. We have confirmed this (14). Nonetheless, one cannot make large changes in blood volume within 7 seconds. We do not know, unfortunately, what the pressure-volume relationship is at the instant the volume is changed. The

Sagawa and Guyton labs seem to start timing the changes after the volume change is made, but it would seem this is not reasonable. But then, one should not start timing at the beginning of the volume change, either. Nonetheless, with some extrapolation, it would appear that a hemorrhage of about 20 ml/kg in a matter of seconds would reduce the mean circulatory filling pressure to near zero and a transfusion of about equal volume would increase it to about 20 mmHg. These data provide the opportunity to make another interesting point: Even though an instantaneous hemorrhage of 15 to 20 ml/kg would bring the MCFP and thus cardiac output to zero, it is possible to hemorrhage a dog over a period of one half-hour to 50 to 60 ml/kg, and it survives. Why is not a 20 ml/kg hemorrhage always fatal? Where does the blood come from? The answer is that some comes from reflex venomotor constriction, but quantitatively more important, during the half-hour to hour there is massive transfer of fluid from the extravascular space to the vasculature. The passive recoil of the veins due to their elastic components is not a factor here, because this accounts for their initial change in volume of the 15-20 ml/kg. Because it is virtually impossible to change the volume of the vasculature and measure the pressure simultaneously within a mass of tissue, it is difficult to get an unequivocal measure of the pressure-volume relationship. We are technique limited.

A concluding figure is the 3-dimensional maze of Figure 11. The total blood volume is on the horizontal axis and is change from control. The MCFP, which determines the venous return and the distending force on the capacity vessels, is on the vertical axis. Time is represented as going toward the back. First of all, notice the stippled plane which represents the change in volume, as a function of time, required to hold the MCFP constant after a sudden change in MCFP. We do not have data at time zero, but as discussed previously, the changes are representative from a half-minute to 5 minutes and include both reflex changes and fluid shifts. At the top of the figure, the wild trajectory is a more definitive measure of the reflex changes. We have found that if we suddenly stopped the heart, determined the MCFP as the pressure at which the large arteries and veins are at the same pressure with zero flow, then this pressure increased (14). At about 20 seconds, we removed volume to bring the pressure to the MCFP found at 5 seconds, and then continually pumped to remove blood to keep the control pressure constant. In our hands, the MCFP of the dog on its side averaged 10.6 mmHg. We continually had to remove blood during the one-minute interval before defibrillation. This totalled about 15 ml/kg. We compared that to the volume removed at the end of one minute after large quantities of hexamethonium were given, and we concluded that the maximum reflex change at one minute was about 9 ml/kg. The reflexes were intact, the dogs were anesthetized with chloralose/urethane, and the cardiovascular stimulations were probably near maximal, since the heart was stopped, the arterial blood pressure was only 11 mmHg, and the chemoreceptors were probably maximally stimulated, since there was virtually no flow. Again, although this volume change is relatively small, a rather small change in central venous pressure can cause a large change in cardiac output.

A complication in this particular study was that the dogs had intact spleens, and so we were not able to delineate the relative role of the spleen compared to the remainder of the vasculature. Since the spleen of a dog is relatively much larger than that of man, maybe active venoconstriction in man is small. We do not yet have complete data on the reflex control of liver blood volume, although the work of Brooksby and Donald (3) and that of Hainsworth (8) would suggest that it is highly significant. Active reflex venoconstriction of skeletal muscle seems to be insignificant (13). The intestinal bed may be more important.
Limitations In The Methods Used To Study Vascular Pressure-Volume Relationships

One of the major reasons why our information on the physiology of the veins is still uncertain and scanty is that the techniques used have grave problems. The most clear cut approach is that of direct observation of the capacity vessels. This approach not only includes optical visualization, but also the use of ultrasound or x-ray or even the application of strain gauge arches or linear variable differential transformers to monitor change in diameter. In general, this approach is difficult to apply to small vessels within a mass of tissue, but that's where most of the blood is. Furthermore, with these direct observations on either large vessels or those at the surface, we cannot be assured that the data so obtained are representative of all vessels.

The plethysmograph — or the use of weighing — is the classic approach to the study of changes in tissue volume and so by inference vascular volume. One major disadvantage is that it measures only the change in volume. Further, it can be applied only to limbs of people. Nonetheless, the noise level can generally be made low, precise measures can be made, and rapidly responding systems have been designed. Another disadvantage of the plethysmograph is that blood leaks are included in the volume changes, as are secretions, and most importantly, transcapillary fluid movement across the capillaries.

The tissue radioactivity monitoring technique, in which the blood albumin is labelled with radioactive iodine or red blood cells are labelled with radioactive chromium, provides a measure of the intravascular volume, if one can assume that the activity measured within the observable space of the detector is proportional to the amount of blood. This does give a measure of total blood volume, but calibration is uncertain because this usually involves placing a unit volume of blood on a planchette and moving it into the observable space of the detector. Unfortunately, the detector geometry is rarely uniform in either the axial or radial direction.

The indicator mean-transit-time (MTT) approach is another technique that provides a direct estimate of contained volume (Fig. 12). If we know the MTT of the indicator through the tissue and multiply this by flow, a measure of volume is obtained. The indicators must be injected into the arterial bed and must be mixed uniformly across the inflow, and then detected in the outflow. Radioactive techniques have been used. In addition, dye densitometers can be used to sample the mixed outflow. The classical approach to MTT determinations is to use a nearly instantaneous slug injection of the indicator, but this presents serious problems because it dilutes the blood and can seriously change the hemodynamics. We have found that a step input of indicator (C) provides a more physiologic measure. The concentration on the inflow and outflow have been monitored and the MTT is defined as the integral of the difference between the outflow concentration and the asymptotic value, divided by this asymptote value. Ken Zierler, (20) among others, has provided useful theory. The major advantage of this technique is that one can get an absolute measure of volume, and, as a consequence, can then only determine the pressure-volume relationship for compliance, but also can obtain a measure of the unstressed volume change. As indicated above, a measure of this is essential if one is to understand venous physiology thoroughly. Although the technique can be used with tissue in the body, the volume of distribution of albumin is larger than that of erythrocytes, and the technique does not measure a volume in which there is no flow. Because uniform mixing of indicator with blood is essential, the technique is not easy to apply.

\[ MTT = \frac{1}{c_{\text{max}}} \int_{0}^{\infty} (c_{\text{max}} - c_{t}) \, dt \]

Fig. 11. Changes in total-body vascular pressure-volume relationship as a function of time after a change in volume (stippled areas) or in response to 1 min of zero cardiac output and near zero arterial pressure (top trajectory). Chloralose anesthesia. Dogs. Modified from Rothe, Circ. Res. 38:705, 1976, Fig. 2.

Fig. 12. Indicator mean-transit-time (MTT) approach to estimating total contained vascular volume. A. Schematic. B. Slug injection of indicator. C. Step input of indicator and equation for calculating MTT.
direction only. Furthermore, it can be used only in situations where pressures at both ends of the constant, flowing stream are available. This problem is not unique to the resistance approach, for indeed, a measure of capillary pressure within the mass of tissue has hindered not only our understanding of venous physiology, but also that of fluid exchange. To assume that 80%, 86% or 90% of change in venous pressure is reflected to the capillary vessels may be reasonable, but we do not have adequate measures to validate this for vessels within the mass of tissue, such as skeletal muscle or liver.

To measure the pressure-volume relationship of the total body, there are two general approaches in use: the pump bypass technique and the mean circulatory pressure approach.

With the pump bypass/reservoir technique, the great veins are cannulated and are emptied into a reservoir at a pressure set by the height of the outflow cannula (Fig. 13A). Blood from this reservoir is pumped into the right heart at a constant rate. A change in outflow (central venous) pressure leads to a change in contained volume of the blood in the vasculature. It is assumed that the resulting change in reservoir volume is equal and opposite to the change in the vascular volume. This approach assumes a constancy of flow and also assumes a constancy of vascular resistances, or at least that the resistance changes are proportional in response to reflex changes or infused drugs. With a constancy of flow and resistance, then a change in venous pressure will be reflected equally throughout the entire vascular system. If the resistances are not constant or proportional, then flow will increase to some tissues and decrease to other tissues, so that the pressure changes will not be the same throughout the body as the central venous pressure is changed. As a consequence, there may be an unequal, passive redistribution of volume (see Fig. 5). This may be a somewhat subtle point, but it is an important pitfall. Compliance is then estimated as the ratio of change in the reservoir volume to that of the imposed change in pressure. If the venous outflow pressure and cardiac output are held constant, then a change in venomotor tone can be detected as a change in reservoir volume without a change in pressure. Under these conditions, it is possible to detect changes in unstressed volume without a change in compliance. This conclusion is valid only if, using a subsequent set of experiments, the compliance did not change under the conditions used. The major problems here are that the technique: 1) does not provide a direct measure of unstressed volume, but only changes in volume. 2) It requires major surgery, since total bypass is required.

A variant of the pump bypass approach is to use a closed system (Fig. 13B). Here, instead of changing the outflow pressure, the blood volume is changed by a known amount and the resulting change in central venous pressure is measured. If one can assume that: 1) the change in central venous pressure is transmitted equally throughout the body; 2) the imposed volume change has been distributed throughout the system proportional to the compliances, and 3) flow is everywhere constant, then the total vascular compliance is the ratio of imposed volume change to the change in measured pressure.

Except for the problem of trauma of preparing the animal, these approaches are probably the most powerful for estimating in situ capillary vessel characteristics. However, they measure (as with other techniques) total vascular capacitance, not just venous capacitance. As a consequence, one must assume that the capacitance of the arterial system is negligible or make corrections for changes in the arterial bed.

![Fig. 13. Pump by-pass approach (constant flow) to estimating vascular compliance or change in unstressed volume. A. Reservoir approach, measuring the change in reservoir volume in response to a step change in venous pressure. B. Constant volume approach, measuring the change in vascular pressure in response to a change in vascular volume.](image)

Finally, the mean circulatory filling pressure approach, developed by Arthur Guyton and his colleagues, involves stopping the heart by fibrillation. In the top panel of Figure 14, the arterial pressure drops because a pump was used to transfer blood rapidly (2 l/min) from the aorta to the veins. The central venous pressure increases and reaches a plateau level. In the third panel down, this pressure is amplified and averaged. The difference in pressure between artery and vein can be brought to the constant and equal value by about 3 seconds. After another 3 to 5 seconds, to verify that a plateau has been reached, the heart is defibrillated and arterial pressure returns to normal within another 5 seconds. The stoppage of the heart and blood flow requires only about 7 to 10 seconds and so is a rather atraumatic procedure, for even after 20 or 30 of these maneuvers over a period of several hours, the mean arterial pressure of dogs has been found to be of the order of 120 mmHg and the cardiac

![Fig. 14. Mean circulatory pressure technique. From Drees and Rothe, Circ. Res. 34:360, 1974, Fig. 1.](image)
outputs over 100 ml/kg-min (15). The pressure-volume relationship is estimated by assuming that the MCP, after the blood volume change, is at the same pressure as in the capacity vessels, even before the heart is stopped. The assumption is reasonable, since certainly a pressure of 11 mmHg is less than capillary pressure and more than the central venous pressure under normal conditions. Some error is present, however. If after fibrillation, blood is not pumped from artery to vein to reach equal pressures within 7 seconds, then reflex venoconstriction may change the value and so confuse the meaning of the data. The mean circulatory approach is also uncertain in that the pressures may not be uniform through the cardiovascular system by 5 seconds, although a slight error on the arterial pressure side will not be serious. Of graver difficulty is the fact that in determining the pressure-volume relationship, it is not possible to change the volume instantly and, during the time of equilibration for the volume change, reflexes and fluid volume shifts can occur.

In summary, we have many techniques to measure reflex changes in capacity vessel pressure-volume characteristics. These rely on many assumptions. The techniques are all in one way or another — faulted because they require anesthesia or trauma, or they do not adequately measure pressure and volume, or do not measure them simultaneously, or representative vessels may not be available for study. The reflex control of the capacity vessels is only partially understood.

ACKNOWLEDGEMENTS

Many important studies have not been mentioned because of limitations of time and space. Since the lecture, several helpful reviews have become available, including those of Vanhoutte and Janssens (19), Hainsworth and Linden (9) and Karim et al (12). I gratefully acknowledge the help of my colleagues in these studies: T. Lesh, J. Drees, B. Johns, T. Bennett; the expert secretarial assistance of Helen Glancy and the support of the IUMC Medical Illustrations Department and Public Health Service grant HL7723.

REFERENCES


INTERNATIONAL SYMPOSIUM ON REGENERATIVE GROWTH PROCESSES AND THEIR CLINICAL APPLICATIONS

The Symposium will be held on September 26, 27, 28, 1979 in Syracuse, New York. It is being organized with the following aims: 1) To accurately define the present state of knowledge in regenerative research, 2) to facilitate the exchange of information between the basic scientist and the clinician, and 3) to identify promising areas of future interdisciplinary research. The program will comprise of presentations by 25 nationally known Faculty. For more information write to: Program Assistant, Office of Graduate and Continuing Education, State University of New York, Upstate Medical Center, 750 E. Adams St., Syracuse, NY 13210. Tel: (315) 473 4607

SPECIAL WORKSHOP
WHITE NOISE ANALYSIS OF PHYSIOLOGICAL SYSTEMS

The special workshop will be held in Los Angeles on June 25-29, 1979. Its purpose is a lecture-demonstration course for physiologists and engineers in the use of multiple, continuous and discrete random inputs for the quantitative analysis of physiologic systems. For information write to: White Noise Workshop Dept. of Biomedical Engineering University of Southern California University Park Los Angeles, CA 90007 (213) 741 6708
Although there have been reports in the clinical literature for at least 40 years suggesting that the deep layers of the left ventricle are more susceptible to ischemic injury than the superficial layers (12), only in the past 15 years has a concerted effort been made to document this experimentally and to establish the physiological basis for uneven perfusion or uneven ischemic metabolic changes in the wall of the left ventricle. This effort has provided some meaningful new insights, not only into the pathophysiology of myocardial ischemia, but into the physiology of the normal heart as well. My purpose at this time is to review briefly some of what has been learned during these past 15 years on the state of and regulation of blood flow and energy metabolism in different layers of the intact left ventricle. As is often the case in research, work on this problem has resulted in a number of conflicting findings, and part of my task will be to point out areas of disagreement and to suggest possible reasons for them.

To begin, much of the impetus for studying this problem can be traced back to the work of Kirk and Honig, who, in 1964, published their novel findings on blood flow distribution and tissue oxygen tension in the normally perfused canine left ventricle (23). A brief description of that work is as follows: An open chest dog preparation was used in which the left main coronary artery was cannulated and perfused from the carotid artery at a constant flow rate. Tissue blood flow was assessed in the superficial and deep layers of the ventricle by the hydrogen clearance method. That is, small volumes of fluid containing \(^131^I\) labeled sodium iodide were injected via 30 gauge needles directly into the myocardial wall at different depths, and the clearance of \(^131^I\) from the depot sites was monitored externally. The data from 19 paired observations indicated that the mean half time of clearance of the isotope was 25% longer in the deep compared to the superficial layer, which was interpreted as evidence of a 25% slower blood flow rate in the deep compared to the superficial layer. In these same experiments oxygen tension was also estimated in the outer and inner ventricular layers, employing bare platinum wire electrodes in some animals and a membrane covered Clark type electrode in others. The results indicated that oxygen tension was substantially lower in the inner ventricular layer.

In a companion study on tissue pressure in different layers of the ventricle, these same investigators obtained evidence of a systolic intramyocardial tissue pressure gradient increasing from epicardium to endocardium (22). It was postulated that this gradient in tissue pressure, by acting as a nonuniform type of coronary extravascular resistance, produced gradients in blood flow and oxygen tension in the ventricular wall. The possibility was raised that under physiologically stressful conditions a major fraction of the energy need of the inner layer would be met by anaerobic glycolysis.

This evidence of relative subendocardial underperfusion and nonhomogeneous oxygen tension in the wall of the normal left ventricle was subsequently supported by the work of a number of other investigators. For example, Winbury and his associates, using the hydrogen clearance method to measure regional myocardial blood flow and the polarographic method to measure tissue oxygen tension, obtained results very similar to those already described (34, 37). Quantitative results obtained from several laboratories showing a relatively lower inner layer oxygen tension are presented in Table 1. The results from Whalen's laboratory deserve special comment. Whalen's electrode is capable of measuring intracellular oxygen tension, and the relatively low values shown are those of intracellular oxygen tension. Also, the terms outer and inner layers must be qualified in reference to that work since both measurement sites were relatively superficial in the ventricular wall. The so-called inner layer site was actually only a few millimeters below the myocardial surface instead of at the more usual inner third or fourth of the ventricular wall.

**Table 1**

<table>
<thead>
<tr>
<th>REFERENCES</th>
<th>OUTER (MM Hg)</th>
<th>INNER (MM Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moss, 1968 (29)</td>
<td>18.0 ±2.3 (S.E.)</td>
<td>10.0 ±1.3*</td>
</tr>
<tr>
<td>Winbury, et al., 1971 (17)</td>
<td>25.7±2.1</td>
<td>16.5±1.9*</td>
</tr>
<tr>
<td>Whalen, et al., 1973 (36)</td>
<td>9.6±1.6</td>
<td>4.6±1.0*</td>
</tr>
</tbody>
</table>

*INTERLAYER DIFFERENCE STATISTICALLY SIGNIFICANT*

A conceptual model of blood flow regulation within the myocardium suggested by all of these findings is one in which the primary determinant of blood flow in the inner ventricular layer is coronary extravascular resistance and not coronary intravascular resistance. A model is suggested in which the arterioles in the inner ventricular layer are maximally dilated and, therefore, incapable of further dilation in the event of an increased energy demand or a reduced coronary perfusion pressure. Thus, this model predicts that the inner ventricular layer would be highly susceptible to an imbalance between oxygen supply and demand. Further support of this model has been obtained in other types of studies. Relatively high inner layer glycogen levels, phosphorylase activity, and other glycolytic enzyme activities have been reported (21,25) and suggested as evidence that the inner ventricular layer is metabolically adapted to function at a reduced tissue oxygen tension. Recently, Allison and Holsinger reported finding significant transmural gradients in high energy phosphate compounds and lactate in the normal canine left ventricle which they offered as evidence of "a relatively reduced oxidative capacity and increased glycolytic reserve in the normal left ventricular subendocardium" (1).
routinely yield inner to outer blood flow ratios that are equal to or greater than 1. However, an early recognized problem with this method is that the transmural distribution of microspheres is size dependent and there is no way of knowing a priori which microsphere size, if any, yields the correct inner to outer blood flow ratio. In studying this problem further, several investigators have shown that the transmural distribution of microspheres with a diameter of 9 μm or less is very similar to that of various diffusible indicators which, because of their different physical properties, are not subject to the same types of anomalous rheologic behavior in the coronary circulation as are microspheres. Although there is some evidence that 15 μm microspheres should be included in this category (6), the inner to outer flow ratio obtained with 15 μm microspheres is usually greater than that obtained with diffusible indicators or with the smaller microspheres (33,38). 

Data obtained in our laboratory comparing the distribution of 9 μm microspheres with that of the highly diffusible substance, 125I iodoantipyrine, are shown in Fig. 1. Both substances were thoroughly mixed in an arterial blood reservoir and administered simultaneously into the cannulated left main coronary artery of the open chest dog for 1 minute. Experimental maneuvers were performed to vary the inner to outer blood flow ratio over a wide range of values. Each data point represents results obtained in a single animal. A high degree of correlation of the inner to outer ratios for the two substances is noted (r = 0.98). However, the slope of the regression line suggests a minor difference in the distribution of the two substances over the range of values obtained. Assuming the antipyrine data to be the more correct for flow distribution, the results indicate that 9 μm microspheres have a slight tendency to underestimate the inner to outer flow ratio at the lower end of the scale and a slight tendency to overestimate it at the higher end of the scale. Virtually identical results to these were obtained in some more recent studies in which either a diffusible indicator or microspheres were used in Table 2. In no study was the ratio significantly less than 1, and in 2 it was significantly greater than 1. The study by Cobb et al. (7) was performed in awake, resting dogs with heart rates averaging 70 beats/min.

![Fig 1](image-url)

**Fig 1** Relationship between inner to outer ratio of 125I iodoantipyrine and 9 μm microspheres obtained in 22 dogs. Dashed line = line of identity. Solid line = regression line.

Historically, evidence favoring a uniform transmural distribution of blood flow in the normal left ventricle was available prior to the development of the microsphere method. In 1967, Moir and De Bra (28), and in 1968, Griggs and Nakamura (15) studied the uptake of diffusible indicators in the left ventricle of the open chest dog and obtained inner to outer ratios that were not significantly different from unity under control conditions. The mean ratio values obtained in these earlier studies along with those obtained in some more recent studies in which either a diffusible indicator or microspheres were used are presented in Table 2. In no study was the ratio significantly less than 1, and in 2 it was significantly greater than 1. The study by Cobb et al. (7) was performed in awake, resting dogs with heart rates averaging 70 beats/min.

**Table 2**

<table>
<thead>
<tr>
<th>Inner to outer ratios for diffusible indicators and microspheres obtained under control conditions in various studies.</th>
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<tbody>
<tr>
<td>Reference</td>
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<tr>
<td>Moir &amp; De Bra, 1967 (28)</td>
</tr>
<tr>
<td>Griggs &amp; Nakamura, 1968 (15)</td>
</tr>
<tr>
<td>Tripp, et al., 1977 (32)</td>
</tr>
<tr>
<td>Tripp, et al., 1977 (32)</td>
</tr>
<tr>
<td>Bueckert, et al., 1972 (6)</td>
</tr>
<tr>
<td>Cobb, et al., 1974 (?)</td>
</tr>
<tr>
<td>Holtz, et al., 1977 (19)</td>
</tr>
</tbody>
</table>

* Difference from unity statistically significant.
Data obtained in various laboratories on normal metabolite levels for the canine left ventricle are presented in Tables 3-5. Studies were selected in which a tissue sample was procured from the intact heart and not from an isolated heart preparation. Metabolite levels for the outer and inner ventricular layers are shown, along with the calculated inner to outer metabolite ratios. Comparison of creatine phosphate data (Table 3) obtained from 5 independent laboratories indicates a lack of agreement concerning the difference found between the outer and inner layers for this metabolite. In studies from 2 laboratories the outer-inner layer difference was not statistically significant (p>0.05); in studies from the other 3 the inner layer level was significantly lower than the outer layer level. A substantial variation occurred in the inner to outer metabolite ratio, which ranged from 1.0 to 0.67. Comparison of the adenosine triphosphate data (Table 4) obtained from the same studies indicates better, but not complete, agreement among laboratories. In studies from 4 of the 5 laboratories, the difference between the outer and inner layer was not statistically significant. In the study from the remaining laboratory the inner layer level was significantly lower than the outer layer level. Table 5 contains myocardial tissue lactate data obtained in studies from 4 laboratories. Also included are additional data from other studies conducted in our laboratory since 1971. Comparison of the results obtained from different laboratories again indicates a lack of complete agreement concerning the outer-inner layer metabolite difference. In studies from 2 laboratories the lactate level in the inner layer was significantly higher than that in the outer layer. In studies from the other 2 laboratories, which includes our own laboratory, the outer-inner difference was not statistically significant. Comparison of the data obtained in our laboratory between 1971 and the present demonstrates a progressive reduction in the absolute tissue lactate levels through the years. We attribute this to periodic modifications in technique which resulted in progressively shorter tissue sampling-freezing times. One factor affecting the absolute tissue lactate level that might account for some of the variability among laboratories is the arterial blood lactate level. Animal preparations with elevated blood lactate levels tend to have elevated myocardial tissue lactate levels under otherwise normal experimental conditions. One factor that probably can be ruled out is the tissue sampling site. We have obtained essentially the same metabolite data for tissue samples procured from different locations in the ventricle, including the posterior wall when care was taken not to twist the heart in preparation for sampling. The present lack of agreement among laboratories concerning the transmural distribution of these metabolites in the normal left ventricle poses a similar problem to that noted for blood flow. Additional studies, preferably by a number of different investigators, might help to resolve this issue.
TABLE 5
REGIONAL MYOCARDIAL LACTATE LEVELS
(µ moles/g)

<table>
<thead>
<tr>
<th>REFERENCES</th>
<th>OUTER</th>
<th>INNER</th>
<th>I/O</th>
</tr>
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<tbody>
<tr>
<td>Ofie, 1976 (30)</td>
<td>1.80±0.26</td>
<td>2.60±0.68</td>
<td>1.44</td>
</tr>
<tr>
<td>Ichihara &amp; Abiko, 1975 (20)</td>
<td>2.24±0.21</td>
<td>3.18±0.19*</td>
<td>1.42</td>
</tr>
<tr>
<td>Allison, et al., 1977 (2)</td>
<td>0.99±0.01</td>
<td>1.67±0.03*</td>
<td>1.69</td>
</tr>
<tr>
<td>Griggs, et al., 1971 (17)</td>
<td>0.30±0.16</td>
<td>1.07±0.13</td>
<td>1.09</td>
</tr>
<tr>
<td>Griggs, et al., 1973 (14)</td>
<td>0.84±0.10</td>
<td>0.39±0.15</td>
<td>1.06</td>
</tr>
<tr>
<td>Griggs, et al., 1974 (13)</td>
<td>0.55±0.04</td>
<td>0.36±0.09</td>
<td>1.09</td>
</tr>
<tr>
<td>Dunn &amp; Griggs, 1975 (8)</td>
<td>0.36±0.06</td>
<td>0.35±0.04</td>
<td>0.97</td>
</tr>
<tr>
<td>Dunn, et al., 1973 (11)</td>
<td>0.30±0.02</td>
<td>0.30±0.02</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* Interlayer difference statistically significant

Table 6
Effects of Various Experimental Interventions on Regional Myocardial Lactate to Pyruvate Ratios

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Layer</th>
<th>outer</th>
<th>inner</th>
<th>I/O</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Control Conditions (17)</td>
<td>region</td>
<td>9.3±1.0</td>
<td>9.3±0.8</td>
<td></td>
</tr>
<tr>
<td>II Moderate Coronary Constriction (17)</td>
<td>region</td>
<td>9.1±1.9</td>
<td>7.3±1.6</td>
<td></td>
</tr>
<tr>
<td>III Severe Coronary Constriction (16)</td>
<td>region</td>
<td>39.2±0.5</td>
<td>113.5±7.2*</td>
<td></td>
</tr>
<tr>
<td>IV Beta Adrenergic Stimulation (17)</td>
<td>region</td>
<td>7.0±1.4</td>
<td>7.1±1.1</td>
<td></td>
</tr>
<tr>
<td>V Moderate Coronary Constriction Plus Beta Adrenergic Stimulation (17)</td>
<td>region</td>
<td>25.6±6.4</td>
<td>36.9±7.2*</td>
<td></td>
</tr>
<tr>
<td>VI Moderate Aortic Stenosis (14)</td>
<td>region</td>
<td>13.8±1.7</td>
<td>14.5±3.1</td>
<td></td>
</tr>
<tr>
<td>VII Moderate Aortic Stenosis Plus Beta Adrenergic Stimulation (14)</td>
<td>region</td>
<td>20.0±3.1</td>
<td>45.5±10.3*</td>
<td></td>
</tr>
<tr>
<td>VIII Moderate Aortic Insufficiency (13)</td>
<td>region</td>
<td>10.8±2.1</td>
<td>11.6±1.9</td>
<td></td>
</tr>
<tr>
<td>IX Severe Aortic Insufficiency (13)</td>
<td>region</td>
<td>14.2±4.7</td>
<td>38.7±10.8*</td>
<td></td>
</tr>
</tbody>
</table>

* Interlayer difference statistically significant

Under control experimental conditions the outer inner layer difference was not statistically significant. Similar results were obtained in animals subjected to moderate coronary constriction. This intervention was produced by cannulating the left main coronary artery and constricting the cannula tubing enough to reduce coronary artery pressure (~38%) but not mean coronary blood flow. Different results were obtained when the coronary constriction was severe enough to reduce mean coronary blood flow (~50%). Under these frankly ischemic conditions the lactate to pyruvate ratio was elevated in both the outer and inner layers and a significant interlayer difference was present due to a greater elevation in the inner layer. Beta adrenergic stimulation, produced by an intravenous infusion of isoproterenol, was without effect on the lactate to pyruvate ratio in either layer despite marked chronotropic and inotropic responses of the heart. On the other hand, when this intervention was combined with moderate coronary constriction an elevated lactate to pyruvate ratio was noted in both layers and a significant interlayer difference was observed, again due to a greater elevation in the inner layer. This same pattern was found in the case of moderate aortic stenosis and beta adrenergic stimulation. Moderate aortic stenosis, achieved by tightening a ligature placed around the aorta proximal to the left coronary ostium, was without effect, but when this intervention was combined with beta adrenergic stimulation a significant interlayer difference in the lactate to pyruvate ratio was observed. Finally, moderate aortic insufficiency, produced by displacing the aortic valve leaflets with a special intravascular instrument, was without effect, but when severe aortic insufficiency was produced a significant interlayer difference in the lactate to pyruvate ratio was again noted.

The absence of a significant interlayer difference in the lactate to pyruvate ratio under control and modestly altered experimental conditions has been interpreted by us as strong evidence against the existence of a metabolically important oxygen tension gradient in the normal left ventricle. The findings suggest that transmural blood flow is regulated in a manner that assures a nutritionally adequate blood supply to all layers of the ventricle under both normal and physiologically stressful conditions. This contention is reinforced by recent evidence that pacing the heart at 200 (10) or even 250 bpm (11) has no effect on the levels of creatine phosphate, adenosine triphosphate, or lactate in different layers of the ventricle.

The significant interlayer difference in the lactate to pyruvate ratio observed under the more severely altered experimental conditions clearly demonstrates that the inner ventricular layer is more susceptible than the outer layer to an imbalance between oxygen supply and demand when the autoregulatory capacity of the coronary circulation is exceeded. These positive results confirm, in a completely independent manner, biophysical evidence of a nonuniform transmural force in the rhythmically contracting left ventricle (3, 22). It has been postulated that this nonuniform force consists of several components or stresses (26) which can cause not only uneven perfusion of the ventricle but uneven energy utilization as well.

Tangible evidence of uneven energy utilization in the forcibly contracting left ventricle has been provided from several sources. Results obtained by us (8) indicate that lactate production by the totally ischemic, pressure generating ventricle is uneven and greatest in the inner layer, whereas that by the totally ischemic, fibrillating or empty beating ventricle (9) is essentially equal in all layers. Evidence that myocardial oxygen consumption may be greater in the inner than the outer layer has been reported by two independent laboratories (19, 35). In both cases regional myocardial blood flow was estimated by the microsphere method and regional oxygen saturation in small arteries and veins (or capillaries) was determined in frozen tissue sections using a microspectrophotometric technique. When tissue oxygen consumption was calculated using the Fick equation significantly higher values were obtained in the inner than in the outer layer. The mean inner to outer ratios for oxygen consumption obtained in these two studies were 1.57 (19) and 1.27 (35).

The evidence that energy utilization may be greater in the inner layer provides additional insight into the mechanism for its greater susceptibility to ischemic injury and also raises the interesting possibility that the inner layer may be specially adapted to meet a constantly greater energy need. Specific vascular and cellular adaptations may exist in the inner layer to facilitate greater oxygen transport and chemical energy production. Studies in our laboratory have revealed a small but significantly higher myoglobin content in the inner layer compared to the outer layer (10), and certain transmural differences in mitochondrial membrane fatty acid saturation (31) and mitochondrial respiratory function (24) which could represent adaptations to an uneven energy need.
REFERENCES


BOOK REVIEW


Davson and Segal, distinguished scholars from England, present a complete up-to-date account of how the body controls posture and locomotion. In a well organized fashion, they broaden our knowledge of basic muscle and nervous mechanisms covered in earlier volumes. Hundreds of salient references on some 2000 aspects of neurophysiology as well as many excellent illustrations provide a solid basis for study. Figure explanations under the photographs and drawings tell a delightful story independent of the main text. The reader will enjoy seeing “How the horse runs and how two elephants flee from a hedgehog”. The great depth and experience of the authors, as they meander through broad facets of anatomy and physiology, makes us aware of the years required to compile and write a book of this caliber. Many classical studies show us how we arrived at our present status in physiology without our being bogged down in details that obscure the basic progress. The distinction between general, mammalian and clinical physiology disappear as subjects move from physics and chemistry to clinical syndromes. Complex aspects of neurophysiology integrate into a whole organism that has a strong basis in anatomy.

The book’s exhaustive nature forces readers to be serious students of physiology. They must be fond of the subject and have a good grasp of anatomy to fathom the heavy material presented. The title, Volume 4: “Introduction to Physiology” misleads us because of the book’s advanced character. When the “going gets tough” one can “browse and skip” for best results. The defining of difficult terms reveal concern for the reader but long sentences one after another, weak verbs and many prepositions create poor reading. In my opinion, 90 word sentences become hard to handle. One encounters repeating of critical areas such as the role servo-action plays in correcting movements already centrally planned. The limitations, exceptions and opportunities in physiology receive much attention which would appeal to medical, dental and graduate students. I do not recommend this text for beginning nurses, pre-medical students or paramedical students. A few topics include: Patterns of behavior; muscle activation; sensory apparatus; spindle and tendon-organ control; brain control; neural organization of locomotion.

The reader learns how basic experimental information contributes to a wide spectrum of applied physiology. Experimental findings demonstrate how motor cortex damage produces spasticity which has important clinical implications. Motor defects may impair the executing of tasks seen in growth and mentally retarded children. Many examples show the physiological relationship of body parts. In steering a car, for instance, the authors mention that the corrective feedback come from the eyes. If your car moves a certain distance off-course, a wheel turn makes the required adjustment. Sophisticated animal models were presented for students to study clinical situations. These educational and research models pin point the necessity of laboratory animal preparations in teaching physiology. Davson and Segal’s new outlook should bear much fruit in many years to come. Students will have a common ground to launch an attack upon the physiological unknown.

Robert H. Davis, Ph.D.
Pennsylvania College of Podiatric Medicine
Philadelphia, Pennsylvania 19107
INTRODUCTION

This is the fourth annual collection of abstracts of educational material presented by the Educational Materials Review Board of the American Physiological Society under the direction of the Education Committee. Board members have submitted abstracts of review articles, papers textbooks, books, manuals, handbooks and symposia which they have found valuable in teaching physiology. Selection of items is wholly at the discretion of members and where more than one member chooses to abstract the same material, each abstract is presented. We hope you continue to find this collection useful in teaching physiology.

The previous three collections constituted the entire issue of The Physiology Teacher. This year the abstracts are supplementing a regular issue of The Physiology Teacher Section of The Physiologist.

M. C. Shelesnyak
Executive Editor
The Physiology Teacher

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CELL PHYSIOLOGY


This book is written primarily for the physician or biomedical scientist who has interests that bridge the basic research laboratory and a thorough understanding of pathophysiology of disease processes. Undoubtedly it will be valuable source book for physicians in training and research trainees in physiology and membrane transport, particularly those interested in understanding the basis for many of the adaptations in the cell membrane that are observed in disease. Although the editors were eclectic in selecting included topics, this eclecticism turns out to be one major advantage of the book in that only topics of interest or controversy which have been influenced by recent scientific investigation are included. The clinical disorders are reduced to membrane phenomena which give the reader the most fundamental and contemporary understanding of these processes available. General topics included are cell membrane structure, problems in membrane biology, cell and epithelial transport, and disorders of membrane transport: particular emphasis is given to normal and abnormal renal transport processes. Also included are selected topics in gastrointestinal absorption, excitable tissue function, cardiac conduction, as well as more isolated discussions of problems such as cell volume regulation and the periodic pterylyases. In spite of the cell or membrane biology orientation of this text, each topic is presented in a section of reasonable length which is not burdensome to the reader. Similarly, the sections are nicely focused and understandable. I highly recommend perusal of this text by physiology teachers who undoubtedly will find information of immediate value for the classroom.

David W. Pluth

ENDOCRINOLOGY AND METABOLISM


This 25-chapter volume reports the proceedings of a symposium reviewing and previewing the "state of the art" with regard to these most complex of the molecules known to have hormonal activity. Nine of the papers deal with the presentation of the structural information of human chorionic gonadotropin and the several pituitary glycoproteins (both mammalian and teleost), with the conformational requirements for binding to a ligand and with the subunit mechanism of glycoprotein hormone assembly. This is juxtaposed with findings on the biosynthesis of the non-glycoprotein reproductive hormone, prolactin, which is, however, an important example of another class of hormone messenger molecules. This book will be especially useful for those who wish an up-to-date general review of the important conceptual redirections that macromolecular hormones actually can enter their target cells in vivo and/or act directly on isolated subcellular constituents in vitro. The publication faithfully preserves the original flavor of the discussions, many of which addressed the idea that the mechanism of action of peptide and steroid hormones may not differ as markedly as popular belief, and much of current teaching, states. Consequently, the volume should serve not only as a guide to the rapidly expanding literature in several converging fields but also as a spectacle of the processes through which important conceptual redirections are, sometimes painfully, achieved.

J.M. Nolín and E.M. Bogdanov

DEVELOPMENT AND AGING


Papers presented at this symposium covered changes occurring in the liver during senescence as deduced mainly from experimental studies on animals and, in particular, on the rat. However, a few clinical studies are also included. The changes in the liver will be reviewed include the following: (1) ultrastructural changes; (2) molecular changes in enzymes, chromatin proteins, DNA, and microsomes; (3) protein synthesis changes in the whole tissue, in isolated hepatocytes, and at the subcellular level; (4) biochemical changes in connective tissue; and (5) functional changes in the transfer of organic anions from the plasma into bile, in bile acid secretion, and in bile flow. The paper on chromatin proteins is not an isolated one and in the modulation of immunogenic responses. This book will be especially useful for those who wish an up-to-date general review of age-dependent changes occurring in the liver at all levels of its organization from the molecular to the whole organ.

T.C. Lloyd

CIRCULATION


This volume was written to provide a single text devoted to the mechanics of the entire circulation suitable for advanced students of cardiovascular physiology. Beginning with a presentation of basic laws of mechanics and their applications to deformation and flow, the authors proceed to describe the circulations in those terms. The heart, arteries, veins, microcirculation, and blood are individually considered. Cell and fluid movement, heart valve motion, flow in collapsible vessels, transcillary exchange, and the pulmonary circulation are included. The mathematical treatment could be described as "intermediate"-more than many physiology graduate students can fully appreciate without some review of fundamentals. Nonetheless, the mathematical physicists might like. It is, nonetheless, probably optimum for the intended readership. If used as a research reference by investigators, they may be disappointed by the lack of a complete bibliography covering specific points. Rather than such a bibliography, many, but not all, chapters have brief lists of further reading, usually of a general nature. However, there is cited everything as would be done in a monograph, would have been a Herculean task and not within the expectations for a textbook.

T. C. Lloyd


A second collection of autobiographical vignettes by senior investigators whose research, in the judgment of the editors, helped to establish neuroendocrinology as a discipline. The first volume, which appeared in 1975, was a valuable historical account, although it unfortunately came too late to include contributions by some of the very first "pioneers", including u.w. Harris. This volume, which collects the reminiscences and personal insights of our contemporaries (including the editors), presents equally fascinating insights into the personalities and motivations of the men (no women appeared among the 29 pioneers who are featured) who helped to give the vision of the first "pioneers" to a point where (p. 239) "...pioneering in neuroendocrinology ceased and became the harvesting of a new science." Although there are some significant gaps in this volume also, the book manages to present a highly readable picture of an era in which mutual recognition and interactions (both pleasant and otherwise) among a score or so of coeval young investigators had results important enough to warrant - for two of the contributors the coveted recognition of the Nobel Prize. To the credit of the editors who (sometimes reproaching themselves, painfully) allowed the authors almost total poetic license, these essays should help succeeding generations of students and investigators to understand how the circumstances in which their scientific forebears found themselves led to the events which culminated in discovery. Preferred differently, it adds flesh to the skeleton accounts present in the more formal scientific literature.

E.M. Bogdanov


This second volume of Pioneers in Neuroendocrinology contains autobiographical and research accounts from many of the leading and most still active investigators in the field: Barraclough, Beach, Berr, Doudovan, Brodías, Cross, D'Angelo, Donovan, Rodríguez, Ettkin Fierko, Golung, Greer, Guillén, Kalman, Martini, McCann, Meites, Reilley, Saffran, Schally, and Zuckerman. Each chapter is preceded by a photograph and biographical sketch of the author, and raw data about his personality, goals, ideas, inventions, triumphs, tribulations, and sources of financial support, views of colleagues, etc. Guillén, McCann, Meites, Saffran, Schally, and Schreiber each describe their early efforts to isolate "release factors" from the hypothalamus, and Schally and Guillén tell how they finally succeeded in determining the structure of TRH, LHRH and somatostatin in 1969-1973 which led to Nobel Prizes in 1977. Also included are insights into the role of hypophyseal biogenic amines and other neurotransmitters on pituitary function; negative and positive feedback of target gland hormones on the pituitary and hypothalamus; neuroendocrine control of feedback loops, in the control of thyroid hormones (both mammalian and teleost), with the conformational requirements for binding to a ligand, and with the subunit mechanism of glycoprotein hormone assembly. This is juxtaposed with findings on the biosynthesis of the non-glycoprotein reproductive hormone, prolactin, which is, however, an important example of another class of hormone messenger molecules. This book will be of particular interest to students and investigators in the fields of physiology, endocrinology, pharmacology and medicine.

D.E. Brown

This article is properly listed as a minireview because the literature covered ranges primarily from 1972 to 1977. In contrast, the topics reviewed range from invertebrates to mammals and include numerous aspects of the arctic environment: physiological, behavioral, acclimatization period, temperature, water balance, and nutrition of marine, aquatic and land animals. The review can readily be read and understood, but it is not exhaustive in scope; however, it will help the novice student to identify the scope and provide an introduction into the literature of arctic biology and environmental physiology. Among the references are numerous very recent, some in-depth research papers. The work will be of interest to undergraduate biology majors as well as graduate students and faculty in many subdivisions of biology, engineering, and medicine.

ENVIROMENTAL AND EXERCISE PHYSIOLOGY


This volume reviews the major review papers of the 5th International Symposium on Mammalian Hibernation, it cannot be found in a library as this symposium. The papers review material since the 4th Symposium in 1971. The topic-inclusion in this case covers more than the area of hibernation. The volume includes the areas of molecular, biochemical, and cellular adaptation in natural torpor and also the role of the central nervous system in regulation of dormancy, also approximately one-fifth of the material covers the adjustment to periods of inactivity. The papers review material since the 4th Symposium in 1971. This Symposium on Somatostatin held in Freiburg in September 1977 are reports on experimental work carried out in the contributor's laboratories, but some present more extensive reviews on their subject matter. The papers included in this volume review the basic science of somatostatin and its potential for application in the clinical setting.

GASTROINTESTINAL PHYSIOLOGY


This impressive volume contains a collection of 11 review articles spanning the entire gamut of gastrointestinal physiology. Each chapter represents contributions made by acknowledged experts in their fields, and the overall treatment of subjects adequately meets the expected standards in quality and content. The chapters on Gastrointestinal Motility, Gastrointestinal Hormones, the Pancreatic Pancreas, and Absorption of Lipids are treated exceedingly well. Considering the chapter on Absorption of Water and Ions, the reviewer concludes that this volume contains more information on biliary secretion than in previous volumes.


This paper reviews recent studies on the effect of the new drug, Cimetidine, on basal, nocturnal and food stimulated gastric acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. 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Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on nocturnal acid secretion in duodenal ulcer patients. Dose-response curves showing the effect of increasing doses of Cimetidine and their effect on noc...
A double-blind trial was carried out on 74 patients with endoscopically proven duodenal ulcer at 3 medical centers for 4 weeks. Patients were randomly allocated to either an inert placebo or a large dose liquid antacid regimen: 30ml (144mEq) of Mg-Al or Al hydroxide 1 and 3 hours after meals and at bedtime (7 doses per day). Patients were endoscopically examined at 1 week, 2 weeks, and at the end of this treatment. It was found that freedom from ulcer symptoms (i.e. frequency and severity of pain, nausea, vomiting, inability to work) was a poor predictor of ulcer healing in the first week of treatment: 33% of patients who were symptom-free had healed ulcers while 45% of those with healed ulcers continued to have ulcer symptoms. Placebo-treated patients who smoked were less likely to heal than nonsmokers, but smoking had no effect on healing in the antacid group. This evidence that antacids promote the healing of duodenal ulcers contrasts with earlier studies. The authors suggest that the ineffectiveness of antacids in previous studies might be due to much smaller doses used or choice of antacid (ca carbonate induces rapid and complete neutralization of acid). The writing is simple, direct and lucid, a tribute to the translator, Dr. M.A. Biederman-Theresa, who like to present clinically relevant material in lectures and to all of us who have duodenal ulcers!

P. H. Bogner

This excellent little text about neurophysiology has been revised and enlarged from the previous edition and sensory physiology has been extracted to provide the subject of a companion volume. The topics discussed here include basic structural features of the peripheral and central nervous system, including the neuron. Chapters are devoted to excitation, transmission, reflexes, muscular contraction, motor systems, regulation of motor function, autonomous nervous system, and a new chapter on integrative function. The writing is straightforward and the material is easy to understand, a tribute to the authors, all faculty members of various German universities, who take pains to define terms clearly, utilize a standardized form of illustration in two colors for emphasis based on figures taken from the literature in large part and provide a number of useful study questions with answers in the back. The writing is simple, direct and lucid, a tribute to the translator, Dr. M.A. Biederman-Theresa.

L.M.N. Bach

This review discusses potassium balance in health and disease. The factors influencing the distribution of potassium between cell water and extracellular fluid are discussed first. Data on the distribution of potassium within the body are summarized. The important role of the kidneys in regulating body potassium is briefly discussed. The major part of this review concerns hypokalemia and hyperkalemia: causes, clinical manifestations, and clinical management. The physiological bases for altered function and for proper treatment are emphasized. This readable review is especially recommended for medical students and physicians.

G. A. Tanner

This book is highly recommended for undergraduate students. The writing is straightforward and the material is easy to understand, a tribute to the translator, Dr. M.A. Biederman-Theresa, who like to present clinically relevant material in lectures and to all of us who have duodenal ulcers!

P. H. Bogner

This is a thorough, up-to-date editorial review on potassium transport by epithelial tissues. Much of the new information in this field has come from in vitro microperfusion and in vivo microinfusion experiments on single nephrons. The authors discuss the nature of potassium transport in the proximal tubule, loop of Henle, distal tubule, and collecting duct. It is now clear that clear that these classical nephron segments function as smaller segments which differ in morphologic, biochemical, and functional characteristics. For example, the distal tubule, as defined by micropuncture, represents a distal to four distinct subsegments. The cortical distal nephron (i.e., half of the distal tubule plus cortical collecting duct) is usually most important in regulating potassium excretion. The factors which affect distal secretion are discussed. These are 1) plasma potassium, 2) adrenal mineralocorticoids, 3) acid-base balance, and 4) distal fluid flow rate. Another aspect of potassium handling considered is possible heterogeneity among superficial and deep nephron populations. Data available so far suggest no difference in renal handling of potassium by superficial compared to deep nephrons. The article clarifies what is known about renal tubule potassium transport and what questions are still unanswered. It is highly recommended for teachers and researchers.

G. A. Tanner


Recent evidence for the coupled transport of sodium and chloride in certain epithelial tissues is discussed in this editorial review. Sodium chloride absorption has been found to occur in a number of tissues, examples of which are gallbladder, ileum and the thick ascending limb of the loop of Henle. Entry into the cell is by way of the neutral coupling of sodium and chloride at the luminal border. Sodium is actively pumped out of the cell at the basal lateral borders and chloride leaves passively. A sodium diffusion potential across the tight junction generates the luminal positive potential difference. Elevation of intracellular cyclic AMP inhibits sodium chloride absorption probably at the luminal entry site. Chloride secretion occurs in the ileum, dogfish rectal gland and cornea. The mechanism is similar to sodium chloride absorption except that the neutral entry site for sodium and chloride is located at the basolateral borders. Once chloride has accumulated in the cell, it passively diffuses out of the cell across the luminal border. Cyclic AMP induces chloride secretion by releasing bound intracellular calcium which then increases the conductance of the luminal border to chloride. This article should be of interest to investigators and students interested in membrane transport, and specifically to those concerned with mechanisms of transcellular chloride transport.

P. N. Wells and L. G. Navar


This is a review of the intrarenal handling of potassium by individual nephron segments. Particular attention is placed on the issue of nephron heterogeneity. In regard to this major question, although gaps remain in our knowledge, the authors conclude that the evidence to date does not indicate that potassium is handled differently by superficial nephrons compared to nephrons whose glomeruli lie in the deeper levels of the cortex. In addition to this primary focus of the review, a general update of renal potassium transport is provided in the introduction and details the known features as well as the unknown features of this transport process. In brief, excreted potassium is derived both from a minor fraction of filtered potassium that escapes reabsorption and from a major fraction of secreted potassium. Potassium is also secreted into the descending limb of the loop of Henle in addition to the well-known site of potassium secretion in the thick ascending limb of the loop of Henle. Dr. Marsh states that it is necessary to postulate active salt transport by this nephron segment. Moreover, the last sections of the review would be of value for all those interested in a scholarly and sophisticated analysis of the current state of knowledge concerning intrarenal potassium transport.

Franklin G. Knox


This new book covers the essentials of renal physiology and renal disease in a reasonably sized text. The 22 chapters were written by 18 authors, who are almost all faculty members at the Mayo Medical School. The manuscript was edited by Dr. Franklyn G. Knox. In the first 12 chapters include: history of renal pathophysiology; body composition; embryology and anatomy of the kidneys; renal blood flow; glomerular filtration; tubular transport; acid-base regulation; renal handling of calcium; and renal handling of phosphate; and ureic acid excretion. Special chapters are devoted to the renin-angiotensin aldosterone system, renovascular hypertension, and the role of renal blood flow in certain renal diseases. The remaining chapters are devoted to the pathophysiology and management of common renal diseases—glomerular disease, parenchymal renal disease, renal failure, and urinary tract infection. A final chapter deals with dialysis and transplantation. The text is nicely illustrated. Numerous references to the original literature are provided. The authors have made an obvious attempt to be informative, yet concise, and have written an up-to-date text that can be easily digested by medical students.

G. A. Tanner


This review summarizes current ideas on the permeability of the glomerular capillary wall and on the mechanisms responsible for proteinuria in glomerular disease. The article discusses restrictions to filtration of macromolecules across the normal glomerular wall. The normal glomerular wall contains anionic structural elements which retard the filtration of anionic macromolecules and facilitate the filtration of cationic macromolecules. Restriction of transglomerular passage of various macromolecules on the basis of size and charge by the different layers of the glomerular wall is discussed. The review then considers the effects of glomerular injury on the size-selective and charge-selective properties of the glomerular wall. Recent experimental studies indicate that a loss of fixed negative charges in the glomerular wall is important in glomerular disease. This loss of fixed negative charges has several consequences: 1) reduced restriction to filtration of circulating polyions (hence, albuminuria), 2) loss of foot processes, 3) enhanced mesangial accumulation of circulating aggregates, and 4) decreased affinity for cationic stains. The article includes four figures, two tables, and numerous references. It is highly recommended for medical students, physiologists, and pathologists.

G. A. Tanner


This editorial review consists of a set of questions concerning the urinary concentrating mechanism framed by Dr. Berlenier, and responses by Drs. Kokko and Marsh. The article opens with a brief preface by Dr. Andreoli which provides a background for the discussion. The major unresolved question is the mechanism whereby salt is reabsorbed in the inner medulla. The last 7 chapters consider the role of medullary blood flow changes in the urinary concentrating mechanism. The next questions discussed concern the importance of urea accumulation in the inner medulla. The discussion centers on the extent to which urea affects concentration of NaCl along the descending limb of Henle's loop, and hence whether an entirely passive mode of salt reabsorption along the thin ascending limb is likely. Finally, Dr. Kokko favors the hypothesis that the significance of the special anatomic relations between tubules and blood vessels in the medulla (described by Kris and co-workers) and the possible role of pelvic urine urea as a factor favoring urinary comduction. It is clear that many areas of controversy remain, and that further sound experimental work and mathematical analyses of the countercurrent mechanism need to be done. The article is recommended for teachers and researchers.

G. A. Tanner

This review discusses the means by which the kidney controls sodium excretion. The author discusses tubuloglomerular feedback and autoregulation as a means of controlling filtrate production. The literature pertaining to control of proximal tubular reabsorption during blood volume expansion is reviewed; changes in Starling forces which have been considered a major factor in explaining glomerular tubular balance and the constancy of fractional reabsorption in the proximal tubule is discussed. Information such as changes in hydrostatic pressure and composition of the filtrate; changes in filtrate composition may alter reabsorption by controlling the motility of the brush border of the proximal tubule. Reabsorption rate in the loop of Henle and distal tubule is directly related to the rate of Na⁺ delivery while in the collecting duct reabsorption of Na⁺ is controlled by aldosterone, prostaglandins, bradykinin, angiotensin, and extrarenal natriuretic hormones. Certainly the exquisite fine control of Na⁺ excretion resides within the collecting duct yet to be uncovered. The review should be of interest to medical and graduate student interested in a succinct view of volume regulatory mechanisms in normal and certain pathological disorders in man.

H. M. Randall


The subject of this review is volume homeostasis and how it can be altered by changes in intrathoracic volume. Head-out water immersion has been used as a long duration stimulus to alter intrathoracic blood volume. After identifying the quantitative relationships between immersion and body position, intrathoracic blood volume and cardiac output, the author discusses possible mechanisms which may be responsible for the relationships. The effects of immersion on the renal responses to increases in central blood volume in the hydrated and fluid-restricted subjects was discussed including diuresis and natriuresis. Identification of and coordinating evidence for the controlling mechanisms which regulate the renal responses were also discussed including aldosterone, sympathetic nervous system, aldosterone, the renin-angiotensin system and natriuretic hormones as they influence salt and water output. Because the immersion model is a non-invasive technique which induces changes in blood volume, it can serve as a model for the study of abnormal volume regulation in patients with decompenated cirrhosis, hypotension and aldosteronism. This review can be of value to both medical and graduate students and faculty who wish to better understand the various homeostatic mechanisms in normal and certain pathological disorders in man.

H. M. Randall


This review is concerned with prostaglandins synthesized in the kidney and their roles in effects on the blood vessel and functions. To place within a working framework the various functional effects of the PGs the authors discuss the synthesis and metabolism of PGs in terms of their localization with the kidney; cyclooxygenase which catalyzes the breakdown of arachidonic acid to endoperoxides is present within the intimal cells of the medulla, the lining cells of the collecting ducts and with the walls of the vascular tissue. From the intimal cells the PGs can enter the interstitial fluid and effect both tubular function and renal hemodynamics. PGs produced in the collecting ducts can alter the effects of the AW as well as Na⁺ transport. PGs, particularly the newly discovered prostaclin (PGI₂) is produced in vascular tissue and can modulate renal release and effect renal hemodynamics which can in turn alter salt and water output. The authors also integrate the relationships of the kinins with PGs in the renal diabetic and collecting duct in their role of promoting a natriuresis. It would appear that the prostaglandin system is most important in the hemodynamically stressed kidney thereby aiding in its perfusion. This review of the renal prostaglandins should be of particular interest to investigators who are studying isolated perfused organs and for medical and graduate students who wish to better understand the control of renal hemodynamics and tubular function that are responsible for volume homeostasis.

H. M. Randall


This new film runs for 30 min and reviews the basic structure and function of the human kidney. The importance of the kidneys in regulating the composition and volume of the body fluids is emphasized. Topics considered include: (1) kidney blood supply and structure of the nephron, (2) structure of the glomerular capillary wall, (3) glomerular hemodynamics, and (4) formation of the urine. The latter includes discussion of reabsorption of solutes and water in the proximal tubule, reabsorption of filtered heme, distal acidification, counter-current multiplication, role of antidiuretic hormones, and the renal-angiotensin-aldosterone system. Relatively new subjects are considered, such as the relation between glomerular filtration rate and blood flow, role of negative charges in the glomeruolar capillary wall in restricting the passage of plasma proteins, the paracellular pathway in proximal reabsorption, and the importance of the distal nephron in Na⁺, K⁺, and K⁺ excretion. The film is up-to-date, nicely animated, and covers a lot of ground. It is recommended as supplementary material for first year medical and graduate students.

G. A. Tanner


This film describes tests commonly used in the clinical evaluation of renal function. Three types of tests are described: tests which assess plasma flow rate, tests for assessing glomerular filtration rate (GFR), and tests of tubular function. The renal clearance concept is explained first. Then the measurement of GFR using inulin or creatinine is discussed. The limited value of plasma creatinine and blood urea nitrogen in assessing GFR is presented. The measurement of renal plasma flow using FAN is described next. The measurement of urinary concentrating and diluting ability and the assessment of renal acidifying ability are illustrated. Finally, urinalysis, using reagent strips and microscopic examination of the urine sediment, is considered briefly. The film is nicely animated and presents the latest methods, such as the radioisotopic evaluation of renal blood flow. The application of renal function tests in a clinical setting is illustrated, and for this reason the film will appeal to first and second year medical students. Obviously, a 30 minute film cannot fully describe the bases of all of these tests, but it may serve as a practical supplement to renal physiology lectures.

G. A. Tanner


This article discusses the regulation of sodium balance under normal and abnormal circumstances. The importance of sodium in determining the volume of the extracellular fluid (ECF) and the importance of the kidneys in regulating this volume are emphasized. Afferent mechanisms ("volume receptors") which apprise the kidneys of a change in some aspect of ECF volume are considered. The efferent mechanisms whereby renal sodium excretion is altered are discussed. Situations in which the body is depleted of sodium are listed, and the compensatory mechanisms which aid in the conservation of sodium are discussed. Finally, situations in which there is sodium retention and associated generalized edema are discussed in detail. Current views are presented on the mechanisms involved in salt and water retention in congestive heart failure, hepatic cirrhosis, and nephritic syndrome. Some principles applicable to the therapy of edema states are considered. The article treats a complex subject in a clear manner, and includes several helpful diagrams. Because of the clinical importance of the subject, this review will be especially valuable to medical students and physicians.

U. A. Tanner
This article discusses the mechanisms that effect the transport of electrolytes and water across vasopressin-sensitive epithelia. The role of electrical charge, molecular size and shape, and glomerular blood flow and filtration rate are considered as factors that affect the passage of negatively charged macromolecules.

The model of plasma membrane structure formulated by Singer and co-workers is presented first. Then the importance of ion transport in all cells is discussed. Next, various modes of transport of materials are considered: simple diffusion, facilitated diffusion, and active transport (both primary and secondary). The importance of Na-K-ATPase and of ATP in active transport is considered. Coupling processes in membrane transport are discussed. Such processes are illustrated by the dependence of glucose and amino acid transport on the sodium gradient across the luminal cell membrane in intestine and proximal renal tubule, and by coupling between Na and U transport across various epithelia. The role of the tight junction and intercellular pathway in salt and water transport across epithelia is discussed. Finally, the mechanism of water transport across vasopressin-sensitive epithelia is considered. Recent experiments suggest that transport pathways for water are independent of those for urea and other solutes in such epithelia. The article is illustrated with several cell transport models. It is recommended for undergraduate biology majors, medical and graduate students, teachers, and physicians.

G. A. Tanner

RESPIRATION


This review of the respiratory muscles is presented in three parts which separately consider mechanics, control and pathophysiology. It analyzes "the actions of the various inspiratory muscles and how they are coordinated to inflate the lung and displace the chest wall, the mechanical properties of these muscles, their control, how they are recruited with increasing ventilation and how they are influenced by disease". Although written for clinicians interested in physiology, these reviews (especially the first two) are excellent overviews of newer ideas suitable for use in a graduate course in respiratory physiology, for which it is often difficult to find instructional material on this topic. The bibliography includes 443 references. Part I focuses on chest wall mechanics, including a brief synopsis of the intrinsic properties of the respiratory muscles. Part II (control) reviews both central and peripheral control of breathing without covering in depth the central organization or the transduction aspects of physical and chemical signals. Part III considers disorders of breathing present with both pulmonary and non-pulmonary illnesses and briefly covers evaluation of respiratory muscle function.

I. C. Lloyd

TECHNOLOGY IN TEACHING PHYSIOLOGY


This study guide is intended for use with Guyton's Textbook of Medical Physiology, Fifth Edition. The authors follow the text chapter by chapter, providing cognitive objectives for each specific topic area. These are followed by constant review statements which are designed as multiple choice "fill-in" paragraphs which, when completed by the student, will provide a review of the major concepts in physiology as self-tested by the reader. The authors have resorted to code letters for each fill-in statement which may be useful for the student when his attention is limited to the paragraph under study. However, the same letters are used repeatedly but with different meanings for successive paragraphs which may introduce an element of confusion. Most medical students may prefer a test question scheme based on the National Board question format.

L.M.N. Bach
INFORMATION TECHNOLOGY IN HEALTH SCIENCE EDUCATION.

This comprehensive monograph produced by fifty-two contributors is an assessment of the potential for successful implementation of computer-assisted instruction (CAI) from the perspective of the leaders in the field who are making it work. All aspects of health science education are covered including basic science, medical, dental, allied health, post-graduate, and even patient education. A great variety of hardware approaches is detailed from small "stand alone" machines to international networks. In particular, experience with the Experimental CAI Network sponsored by the Lister Hill Center of the National Library of Medicine is reviewed and excerpts from a previously published evaluation appear as an appendix. Many of the contributors to this volume have been involved, in one way or another, with this ambitious project whose outgrowth, the Health Education Network, Inc., still remains as a viable alternative for accessing CAI programs. The chapters were written in the middle of the decade, hence the new developments of the last three years have not been included. The advent of microprocessor-based technology at a fraction of the cost of even the relatively less expensive minicomputers, serves to reinforce the main theme of the book: computerized medical information systems have been successfully developed in the past, presently, significant improvements are being made in these systems; and in the future, they will become a permanent feature of the health science education scene.

C.S. Tidball

INDEX TO COMPUTER BASED LEARNING, 1970 EDITION. Warm, Anastasia C.

The sixth edition of this catalog of computer-based educational materials represents a substantial improvement over previous versions in both scope and format. The 1976 Edition cataloged 1,837 individual programs; it consisted of a table of contents by subject, 609 pp. of program descriptions and 119 pp. of indices. This new edition catalogs 2,997 individual programs; it contains an enlarged table of contents, 1,012 pp. of program listings and 220 pp. of indices. The 1976 Edition was available either in computer printout, a bulky 11x17" volume, or in microfiche. The present offering consists of three soft-cover volumes which are well-printed and easy to use. An additional index by Program Category has been added. Within the main program descriptions, information is included under 24 characteristics. The addition of the characteristic 'Operating System' to this new edition is an indication of continuing efforts to improve the utility of the catalog. The data is obtained by questionnaire which is a possible source of incomplete information; however, as this compilation becomes more comprehensive and thus more authoritative, program developers who fail to respond will do so at their own loss. The indices show signs of improvement but still need more work; redundant index entries caused by differences in the way respondents submitted information should be eliminated. Nevertheless, this work is without doubt the best source of information on computer-based learning available today.

C.S. Tidball