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Editor's Page

There are two highly controversial issues presented in this issue of THE PHYSIOLOGIST. One is the matter of the increasing number of 10-minute papers and the size of the Federation meetings. Other societies of the Federation are concerned about this growing problem and several have tightened up their rules for accepting abstracts. With every society having rules of varying severity, those with the most severe rules are not prone to accept transfer papers from societies with more lenient rules since they feel it would not be fair to their own members to program papers from other societies while not programming papers from their own members. If transfer of papers from one society program to another, where it may fit much better into a session, is restricted it will mean that there will be more than the usual number of combined session topics (4 or 5 papers on one subject plus 4 or 5 on another). In order to make up well integrated sessions as well as a better orientated program, transfer of papers from one society to another society session is essential. Could thought be given to encouraging all societies to have relatively similar restrictive rules, and increase the number of truly intersociety sessions? This would prevent many overlaps and much hopping around.

The other controversial matter is that of membership requirement in the APS. Liberalization of residency requirement will come before the Society for vote at the Fall meeting. The present Bylaws just state that a person must be a resident of North America, they do not specifically state the length of residency but this has always been interpreted to mean intent of permanent residency. We have had many applications from South American, European and Japanese nationals working in North America for varying periods of time who would like to become members while they are residents of North America and then carry their membership, with the prestige associated with it, back to their native country. Would this be a good policy? How would it affect the status of our honorary memberships? Should a separate caregory of membership be established for these foreign nationals? Our constitution states only one purpose of the Society - "to promote the increase of physiological knowledge and its utilization."

APS BUSINESS MEETINGS
April 15 and 17, 1962

ELECTIONS. Hermann Rahn was elected to the position of President-Elect. J. M. Brookhart was elected to a four-year term on the Council. J. D. Hardy was elected to fill the two-year unexpired term of Hermann Rahn on the Council. All candidates nominated by Council were elected to membership. (See Newly Elected Members - this issue.)

MEMBERSHIP REQUIREMENTS. The Membership Committee recommended liberalizing the residency requirement for membership. (See Membership Requirements - this issue - for present rules.) The purpose of the recommendation was to permit foreign citizens working in this country for two or three years to be eligible for regular membership. The matter will be brought up for vote at the Fall Business Meeting.

PROGRAM. The Program Advisory Committee announced that a brief questionnaire would be sent to all members regarding suggestions for topics, speakers and moderators for symposia; for persons to deliver 30-minute introductory summaries; and for general comments. By this mechanism the Committee hopes to tap new and additional sources of talent.

It was announced that the Federation Proceedings abstract issue for 1963 will be arranged like the program and will have an index. These will be mailed to all members. An abbreviated program will be supplied to all attending the meeting.

PRESENTATION OF PAPERS. Council proposed a change in the Bylaws that would require a member be listed among the authors in order for an abstract to be accepted. The reason for the proposed added restriction was to reduce the number of 10-minute papers. After considerable discussion and many alternate proposals (see Report of Program Advisory Committee - this issue) it was moved, seconded and voted that we retain the right of non-members to present papers without a member co-author but merely member sponsorship.

Additional discussion led to a motion, duly seconded and voted that a person's name could appear only once in the program. This is essentially a very literal interpretation of the present by-law which reads in part as follows:

> At a Spring meeting of the Society... a member or honorary member may present orally; be co-author of; or introduce (sponsor) not more than one scientific paper, except upon invitation of the Council.

In other words a member has one of three choices - give a paper; be co-author of a paper; sponsor a non-member. A member or non-member can have his name appear only once. For example,

two members working together who want both their names to appear on an abstract can present only one paper since one will use the choice of giving the paper and the other will use the choice of being a co-author.

The rule will be strictly enforced for the 1963 Spring meeting.

RELATIONS WITH FEDERATION. There were many suggestions and a great deal of discussion on the types of meetings the APS should have and the relationship of such meetings, if any, with the Federation meetings. It was suggested that APS hold meetings (in addition to the Fall meeting) away from the Federation meetings. A great majority of those present opposed this action. It was finally moved, seconded and voted that the APS continue to meet with the Federation but that Council make a continuing study of the matter.

PUBLICATIONS. The Publications Committee announced the forthcoming Handbooks. The first volume of the Circulation section is off the press and other sections are in preparation.

It was announced that the Society had purchased the Journal of Neurophysiology January 1, 1962.

OTHER ANNOUNCEMENTS.

Council solcited invitations from universities to act as hosts for the 1965 Fall meeting.

Council authorized the APS representatives on the U.S. National Committee to invite the International Union of Physiological Sciences to hold the 1968 or the 1971 International Congress in the United States. The 1965 Congress will probably be held in Japan. Congresses are held every three years.

BOWDITCH LECTURE

President Davenport has chosen Dr. T. Hastings Wilson to deliver the Bowditch Lecture at the 1962 Fall Meeting. The title of his lecture will be "Absorption from the Intestine."

Dr. Wilson is the son of D. Wright Wilson, a retired member of APS. He obtained his M.D. degree from Pennsylvania where he worked with M. H. Jacobs. He worked in the Department of Biochemistry at Oxford, the Department of Physiology at Sheffield, the Department of Biochemistry at the Walter Reed Institute of Research, the Department of Biochemistry at Washington University in St. Louis, and he is now Associate Professor of Physiology at Harvard Medical School. He has been particularly concerned with the use of in vitro methods in the study of the processes of intestinal absorption.

SPRING MEETING STATISTICS

	1961	1962
Total attendance	12,569	14,549
Total number of sessions	270	285
Intersociety sessions	49	54
Movies	14	9
Simultaneous sessions	29	31
Total number of papers	2,815	2,986

APS Abstracts

Total received	847
Transferred to other societies and intersociety	219
Received from other societies	80
Total number of sessions programmed by APS (including Intersociety on Endocrines and Blood)	75
APS simultaneous sessions	5-7

34% of abstracts had members as first authors
28% had members as co-authors
66% of abstracts had non-members as first authors
38% had non-member authors sponsored by members but no members as co-authors.

REPRINTS AND PUBLICATIONS NEEDED

The research library of the Institute of Experimental Medicine and Surgery of the University of Montreal has suffered extensive losses owing to destruction by fire.

In attempting to rebuild the library, scientists are asked to contribute all available reprints of their work, especially those dealing with endocrinology and stress.

Address your contributions to:

Institute of Experimental Medicine and Surgery
University of Montreal
P. O. Box 6128
Montreal 26, Canada

MEMBERSHIP STATUS

April 1962

Active members	1996
Retired members	123
Honorary members	16
Associate members	136
	2271

SUSTAINING ASSOCIATES

Abbott Laboratories, Inc.
Ayerst Laboratories
Burroughs Wellcome & Co., Inc.
CIBA Pharmaceutical Products
Ethicon, Inc.
Gilford Instrument Laboratories
Gilson Medical Electronics
Grass Instrument Co.
Harvard Apparatus Co.
Hoffman-La Roche, Inc.
Lakeside Laboratories
Eli Lilly and Co.
Merck Sharp & Dohme Research Laboratories
Charles Pfizer and Co., Inc.
Riker Laboratories, Inc.
A. H. Robins Co., Inc.
Sherman Laboratories
Smith Kline & French Laboratories
Squibb Institute for Medical Research
Tektronix
The Upjohn Co.
Warner-Lambert Research Institute
Wyeth Laboratories

DEATHS SINCE SEPTEMBER 1961

Clyde Biddulph
Edgar D. Brown (R)
Martin H. Fischer
Harry Greengard
Kenneth K. Jones (R)
Carney Landis
David I. Macht (R)
Irvine McQuarrie (R)
Arthur R. Moore (R)
Wesley T. Pommerenke
Homer W. Smith (R)
Bernard J. Sullivan
Harold G. Wolff

50-YEAR MEMBERS

Samuel Amberg (R)
George Bachmann (R)
Harold C. Bradley (R)
Clyde Brooks (R)
Percy M. Dawson (R)
Joseph Erlanger (R)
Alexander Forbes
Charles C. Guthrie (R)
Philip B. Hawk
R. G. Hoskins (R)
Dennis E. Jackson (R)
Israel S. Kleiner
Frank P. Knowlton (R)
David Marine (R)
J. F. McClendon (R)
Hugh A. McGuigan (R)
Walter J. Meek (R)
Frederick R. Miller (R)

Victor H. K. Moorhouse (R)
Eugene L. Opie (R)
W. J. V. Osterhout
Alfred N. Richards (R)
Andrew H. Ryan
Charles D. Snyder (R)
Torald Sollmann (R)
George H. Whipple (R)
Carl J. Wiggers (R)

NEWLY ELECTED MEMBERS

The following, nominated by the Council, were elected to membership in the American Physiological Society at the Spring meeting, 1962.

FULL MEMBERS

AMES, Adelbert III: Res. Assoc. Biol. Chem., Harvard Med. School.
ASSALI, Nicholas S.: Prof. Obstet. & Gynecol., & Physiol., UCLA.
ASTRUP, Tage: Dir. of Res., James F. Mitchell Fndn., Washington, D.C.
ATTINGER, Ernst O.: Visiting Asst. Prof. Physiol., Univ. of Pennsylvania.
AWAPARA, Jorge: Assoc. Prof. Biol., Rice Univ.
BALFOUR, William M.: Res. Assoc., Visiting Lecturer, Univ. of Kansas.
BARBER, Albert A.: Asst. Prof. Zool., UCLA.
BARKER, Earl S.: Assoc. Prof. Med., Univ. of Pennsylvania.
BARRACLOUGH, Charles A.: Asst. Prof. Anat., UCLA.
BISHOP, David W.: Staff Member, Embryol., Carnegie Inst. of Washington.
BLATTEIS, Clark M.: Chief, Therm. Injury Br., US Army Med. Res. Lab., Ft. Knox.
CAIN, Stephen M.: Res. Physiologist, Asst. Prof. Physiol., USAF School Aerospace Med.
COLE, Benjamin T.: Assoc. Prof. Biol., Univ. of South Carolina.
CONNOR, William E.: Asst. Prof. Int. Med., State Univ. of Iowa.
COPE, Freeman W.: Physiologist, Aviation Med. Accel. Lab., Naval Air Development Ctr.
CORNBLATH, Marvin: Assoc. Prof. Pediat., Northwestern Univ.
DENISON, Mary E.: Co-Dir., Endocrine Consulting Labs.
FINK, Bernard R.: Assoc. Prof. Anesthesiol., Columbia Univ.
FRANK, Nedd R.: Assoc. in Physiol., Harvard School Public Health.
FUSCO, Madeline M.: Asst. Prof. Physiol., Univ. of Michigan.
GASS, George H.: Assoc. Prof. Physiol., Southern Illinois Univ.
GIRERD, Rene Jean: Sr. Scientist, Warner-Lambert Res. Inst.
GOLDSTEIN, Leon: Res. Assoc., Biol. Chem., Harvard Med. School.
GROSS, Warren J.: Assoc. Prof. Zool. & Act. Chmn., Div. Life Sci., Univ. of California.
HEROUX, Olivier P. J.: Assoc. Res. Officer, NRC, Ottawa.
JASPER, Robert L.: Co-Dir., Endocrine Consulting Labs.
KHAIRALLAH, Philip A.: Asst. Staff, Cleveland Clinic Fndn., Res. Div.
KING, James R.: Asst. Prof. Zoophysiol., Washington State Univ.
KLING, Arthur: Asst. Dir. Res., Illinois State Psych. Inst.
KOKAS, Eszter M.: Asst. Prof. Physiol., Univ. of North Carolina.
KOLIN, Alexander: Assoc. Prof. Biophysics, Univ. of California.

KORMAN, Samuel: Res. Collaborator, Brookhaven Natl. Lab.
KRUGER, Lawrence: Asst. Prof. Anat., UCLA.
LOSTROH, Ardis J.: Asst. Prof. Exptl. Endocrinol., Univ. of California.
LUCHSINGER, Peter C.: Chief, Cardio-Pulmonary Physiol. Res., Georgetown Univ.
MARSHALL, Norman B.: Res. Assoc., Nutr. & Metabolic Dis., Upjohn Co.
MARTORANO, Joseph J.: Head, Physiol. Div., Naval Med. Field Res. Lab.
MOULDER, Peter V.: Assoc. Prof. Surg., Univ. of Chicago.
O'BRIEN, Larry J.: Chief, Cir. Physiol. Sect., Civil Aeromed. Res. Inst.
PATLAK, Clifford S.: Mathematician, NIMH, NIH.
POGGIO, Gian F.: Asst. Prof. Physiol., Johns Hopkins Univ.
RAWSON, Kenneth S.: Asst. Prof. Zool., Swarthmore College.
SACHS, Bernard A.: Res. Associate, Montefiore Hosp.
SCHOTTELIUS, Dorothy D.: Res. Associate, State Univ. of Iowa.
SELDIN, Donald W.: Prof. & Chmn., Dept. Int. Med., Univ. of Texas, Southwestern Sch. Med.
SHARP, John T.: Chief, Cardio-Pulmonary Lab., Hines VA Hosp.
SMALL, Melvin D.: Chief, Gastrointestinal Res. Sect., Georgetown Univ.
SPENCER, Richard P.: Asst. Prof. Biophys., Univ. of Buffalo.
STEIN, Myron: Instr. Med., Harvard Med. School, Assoc. Med. Beth Israel Hosp.
STEINETZ, Bernard G.: Sr. Scientist, Warner-Lambert Res. Inst.
STEVENS, Charles E.: Assoc. Prof. Physiol., New York State Vet. Coll.
SWEET, William H.: Assoc. Prof. Surg., Massachusetts Gen. Hosp., Harvard Med. School.
TRAVIS, David M.: Asst. Prof. Med., Pharmacol. & Therap., Univ. of Florida.
VANDER, Arthur J.: Instr. Physiol., Univ. of Michigan.
VERNBERG, Frank J.: Assoc. Prof. Zool., Asst. Dir. Res., Duke Univ.
WEBB, Watts R.: Assoc. Prof. Surg., Univ. of Mississippi.

ASSOCIATE MEMBERS

BARRY, Jeanne Q.: Instr. Physiol., Univ. of Maryland.
EISENMAN, Joseph S.: Instr. Physiol., Univ. of Pennsylvania.
EISENSTEIN, Edward M.: Grad. Student, & Pre-doct. Fellow, Psychol., Physiol., UCLA.
FRAYSER, Katherine R.: Assoc. Physiol., Duke Univ.
GOODFELLOW, Elsie F.: Asst. Prof. Anat., Creighton Univ.
HAST, Malcolm H.: Res. Fellow, NIH, Ohio State Univ.
HEMMINGSEN, Edvard A.: Asst. Res. Physiol., Scripps Inst. of Oceanography.
LENTINI, Eugene A.: Instr. Physiol., Univ. of Oregon.
LEVITT, Melvin: Res. Assoc., The Rockefeller Inst.
NOCENTI, Mero R.: Asst. Prof. Physiol., Columbia Univ.
PAGANELLI, Charles V.: Asst. Prof. Physiol., Univ. of Buffalo.

ROSENTHAL, Fred: Jr. Res. Physiologist II, Univ. of California, Berkeley.
SANTOLUCITO, John A.: Assoc. Prof. Zool., North Carolina State Coll.
SCHAEPPI, Ulrich: Scientist, Worcester Fndn., Massachusetts.
WALTER, Donald O.: Grad. Res. Physiologist & Anatomist, UCLA.
WOOLLEY, Dorothy E.: Postdoctoral Fellow, NSF, Univ. of California.

FUTURE MEETINGS

1962 - Fall Meeting, Univ. of Buffalo, N.Y., Aug. 28-31; Dr. Hermann Rahn, Local Committee

1962 - XXII International Congress of Physiological Sciences, Leiden, The Netherlands, Sept. 10-17
Congress Secretariat, P.O. Box 133, Leiden, The Netherlands

1963 - Spring Meeting, Atlantic City, N.J., Apr. 16-21

1963 - Fall Meeting, Univ. of Miami, Coral Gables, Fla., Sept. 3-6; Dr. Gordon Ring, Local Committee
Celebration of 75th Anniversary of the American Physiological Society

1964 - Spring Meeting, Chicago, Ill., Apr. 12-18

1964 - Fall Meeting, Brown Univ., Providence, R.I., Sept. 8-11; Dr. Walter Wilson, Local Committee
200th Anniversary of Brown Univ.

1965 - Spring Meeting, Atlantic City, N.J., Apr. 10-16

MEMBERSHIP REQUIREMENTS

SECTION 2. Members. Any person who has conducted and published meritorious original research in physiology and/or biophysics and who is a resident of North America shall be eligible for membership in the Society.

Present criteria and interpretations:

Publications - at least one physiological paper, beyond the thesis, of which the applicant is the major author.
Residency - interpreted as permanent resident of North America, a citizen - or intent to become a citizen. (Many feel the intent of permanency of residency should not be required and that limitations should not be restricted to North America but should include all of the Western hemisphere.)
Other factors considered - publication in APS journals; attendance at APS meetings; intent to remain in physiological work; interest in Society activities; sponsoring letters; etc.

Mechanics and time factors:

Applications signed by two sponsors and accompanied by letters of recommendation from the sponsors are submitted to the APS central office. Those received before February 15 and after July 15 are duplicated and sent to members of the Membership Committee who independently vote on each candidate. The Committee meets prior to the Council meeting at the Spring meeting and finalizes its recommendations to Council. Council considers the Committee's recommendations and approves a list of nominees to the Society. This list is enclosed in the next issue of THE PHYSIOLOGIST to all members and placed on a ballot for formal election at the Fall meeting. Applications received between February 15 and July 15 are acted upon by the Committee and Council at the Fall meeting and those nominees selected are placed on the ballot for election at the following Spring meeting.

An application may be deferred pending more information or further fulfillment of some criteria. In such cases the sponsors are notified and asked to inform the applicant and encourage him to meet the criteria as soon as possible. It is the sponsor's responsibility to see that the applicant's name is presented when the criteria are fulfilled by submitting a deferred application form.

1961 FISCAL REPORTS

SOCIETY OPERATING FUND

INCOME	
Regular Membership Dues	$19,000
Associate Membership Dues	430
Sustaining Associates	7,825
Interest on Savings Accounts	1,211
Fall meeting, net	495
President-Elect Tour, net	57
Reimbursement from Federation Spring meeting	1,577
Reimbursement from Grants (overhead)	1,986
Total Income	$32,581
Amount in Savings & Loan as of Dec. 31, 1961	$31,461
Cash in Bank as of Dec. 31, 1961	$14,788
EXPENSES	
Salaries, Social Security, Insurance & Pensions	$10,096
Travel	1,574
Addressing, Mailing & Shipping	1,198
Telephone and Telegraph	82
Supplies and Duplicating	1,399
Equipment	696
Depreciation on Equipment	252
Dues to Federation	7,636
Dues to AIBS	1,858
Incidental Expenses	73
Business Office Service Charge	3,264
Total Expenses	$28,128
Excess of Income over Expenses	$ 4,453

PUBLICATION OPERATING FUND

INCOME	
Subscriptions	$217,021
Sale of Reprints	67,572
Other Publication Sales	8,083
Advertising Income	10,010
Author Charges	15,400
Miscellaneous Income	507
Total Income	$318,593
EXPENSES	
Salaries, Social Security, Insurance & Pension	97,200
Printing and Engraving	179,160
Other Personal Services	3,159
Supplies and Duplicating	4,076
Communications, Shipping and Travel	22,416
Depreciation on Furniture and Equipment	1,426
Rental	7,028
Incidental Expenses	2,764

Business Office Service Charge	50,080
	$367,309
Less Allocations to Publication Inventories, etc.	14,385
Total Expenses	$352,924
Excess of Expenses over Income	$ 34,331

PUBLICATION CONTINGENCY AND RESERVE FUND
as of Dec. 31, 1961

Cash on Hand (with Wood, Struthers & Co.)	$5,233
Bonds	182,600
Preferred Stock	45,200
Common Stock	510,700
Quoted Market Value	$743,733
Dividends and Interest paid to APS in 1961	$ 24,603
Principle paid to APS in 1961	$ 70,000

Amounts paid to APS were used to purchase the Journal of Neurophysiology and offset losses of Publication Operating Fund.

FOREIGN SCHOLARS

The Committee on International Exchange of Persons of the Conference Board of Associated Research Councils now has for distribution a list of foreign scholars available for remunerative positions in American universities and colleges during the academic year 1962-63. This list is compiled annually by the Committee and includes information about scholars recommended by the U.S. Educational Commissions and Foundations abroad. Each scholar is eligible for a Government travel grant covering costs of round-trip transportation to the United States if arrangements are completed for a lecturing or research appointment at an American university or college.

A list and information may be obtained from Mrs. John D. Leary, Program Officer, Conference Board Committee, 2101 Constitution Avenue, NW., Washington 25, D.C.

REPORT OF PROGRAM ADVISORY COMMITTEE

L. L. LANGLEY
W. P. ANSLOW, JR.
R. M. BERNE

The Program Advisory Committee appointed by Council in January 1962, has devoted its efforts to consideration of the following subjects:

A. Means of reducing the number of 10-minute papers at the Spring meeting.
B. Consideration of the number of individuals attending the Spring meeting.
C. Means of improving the 10-minute papers.
D. Initiation and presentation of symposia.
E. Selection of chairmen to give the 30-minute introductory talks.

In order to assist the Committee in its early deliberations, letters were sent to approximately 60 members of the Society soliciting their viewpoints and suggestions concerning the above subjects. About 50 replies were received. The overwhelming majority recognizes that some limitation must be placed upon the number of 10-minute papers which are presented at the Spring meeting. The actual number of individuals who register at the Spring meeting does not, as yet, pose a serious problem. However, if the Federation is to be able to meet in cities other than Atlantic City, or even in Atlantic City, the present rate of increase in the number of 10-minute papers, must be reversed. Almost everyone agrees that considerable improvement in the 10-minute papers, both in content and presentation, is desirable. Most of those who replied to the Committee's letter favor the continuation of symposia and the 30-minute introductory talks, although there were a surprising number of members who saw little value in the symposia, and an even greater number who denounced the 30-minute introductory talks.

The Program Advisory Committee has carefully considered the viewpoints and suggestions which it received from the limited membership canvassed and makes the following recommendations:

A. Means of reducing the number of 10-minute papers at the Spring meeting.
   1. This Committee strongly urges adoption of the proposed motion to change section 4 of Article VII of the Bylaws so that a member could present orally or be co-author of not more than one scientific paper, except upon invitation of the Council. At the prsesnt time, some members have their names on as many as 7 papers. Under the proposed rule this would not be allowed. (See APS Business Meetings for action taken.)

   2. In the event that the proposed rule fails to reduce the number of 10-minute papers sufficiently

it is proposed that a member could present orally or be co-author of not more than one scientific paper once every second year, except upon invitation of the Council.

3. Because some institutions require that an individual be on the program in order to qualify for his expenses to attend the Federation meeting, this Committee strongly urges the President of the Society to write to the Presidents of such institutions in an attempt to relax this requirement which has as its natural result the inclusion on the program of papers that otherwise would not have been submitted.

4. Consideration should be given to the requirement that non-members must attend 1 or 2 Spring meetings in order to qualify to present a paper at a Spring meeting. The purpose of this requirement is to give young scientists added experience before being on the program.

5. Consideration should also be given to the requirement that a member, in order to have the right to be co-author on a paper, must have attended a meeting of the Society at least once in the previous 3 years.

6. The Committee feels it ultimately may be a requirement that a full-length paper be submitted for publication along with the abstract. The paper could be submitted for publication in any appropriate journal. Acceptance of the paper would be necessary in order for the abstract to appear on the program of the Spring meeting, but the preparation of the paper and the knowledge of subsequent editorial review would limit the number of abstracts submitted and should also improve their quality.

7. Consideration should be given to having a limited number of simultaneous sessions at the Spring meeting. The subject matter of each session would be announced at the time of the call for abstracts, and only abstracts that fit into these categories would be accepted. Abstracts on other subjects would probably then be submitted for presentation at the Fall meeting and would thereby improve the Fall meeting.

8. If any combination of the above recommendations fails to produce the desired result of limiting the number of 10-minute papers and improving their quality then it may be necessary to have editorial selection of papers for presentation. If such a step

is taken, it is suggested that a full length paper be required in order to facilitate selection.

9. Some members favor the complete elimination of the 10-minute paper for the Spring meeting. Instead there would be symposia and invited full-length talks. Such a drastic step would certainly reduce the size of the Spring meeting and undoubtedly improve the Fall meeting which would remain open for 10-minute papers.

B. Means of reducing the attendance at the Spring meeting.
   1. It is probably not desirable, at the present time, to limit the total attendance. However, if the number of 10-minute papers were reduced the total attendance would probably also be reduced.

   2. If it becomes desirable to reduce the attendance the meeting could be made open only to members and a limited number of guests sponsored by members.

C. Means of improving the 10-minute papers.
   1. The mimeographed form "Suggestions to Speakers" should be included with the abstract forms sent to all members.
   2. One of the functions of the Committee is to evaluate the program. It is impossible for the three members of the Committee to do this in any complete or satisfactory manner. Accordingly, the Committee strongly urges that the Council appoint chairmen for a two-year period. During the first year of the assignment, the appointee would be assigned to a session at the Spring meeting. It would be his task to evaluate each paper, each presentation, and also to evaluate the manner in which the chairman conducts the session. This would be done anonymously and reported confidentially to the Committee. The Committee would use this information for recommending future chairmen, participants in symposia and chairmen to give 30-minute introductory talks. Such constant evaluation would undoubtedly uncover new talent and operate to give far broader representation in symposia. It should also markedly improve all sessions.

D. Initiation and presentation of symposia.
   1. The Committee is sending a questionnaire to every member of the Society soliciting suggestions for topics and participants for future symposia.

   2. Using the evaluation system proposed above, it is hoped that symposia can be presented which have a high degree of coordination and which will cover an

aspect of physiology dynamically and thoroughly.

3. This Committee deplores the splintering of the Society into sub-groups. Accordingly it is strongly recommended that all symposia initiated by any group for presentation during the Spring meeting be an open session under sponsorship of the Society.

E. Selection of chairmen for 30-minute introductory talks.
   1. The 30-minute talks have proven very popular and this Committee recommends that they be continued.
   2. If the recommended evaluation system is adopted, this Committee should be in a position to broaden and improve the selection of chairmen for this purpose.
   3. A questionnaire is being sent to the membership soliciting suggestions for topics and speakers for the 30-minute introductory talks.

SOCIETY FOR VISITING SCIENTISTS

The Society for Visiting Scientists has changed its address to:

No. 19 Albemarle Street
London, W. 1., England

Sleeping accommodations and restaurant facilities will no longer be available, but members will be assisted in finding reasonbly priced hotels for their visits to London. The information service will be unimpeded and will remain available for all institutions and individuals wanting to use it.

REPORT OF THE COMMITTEE ON USE AND CARE OF ANIMALS

BENNETT J. COHEN

Several important developments affecting animal experimentation and laboratory animal care have occurred recently. The purpose of this report is to summarize these developments for the information of A. P. S. members.

Standards for Laboratory Animal Facilities and Care

The National Institutes of Health has contracted with the Animal Care Panel to draft and publish appropriate professional standards for laboratory animal facilities and care. The purpose of this project is to provide an authoritative reference to assist scientific institutions in providing the best possible care for laboratory animals. The standards will be based on scientific evidence insofar as possible, and on expert experience and opinion. They are being developed around the following principles:

1. The care and management of laboratory animals should be directed by professionally qualified persons.

2. Animal care personnel should be suitably qualified by training and experience in the care of laboratory animals.

3. Physical facilities and methods of care for animals should permit their maintenance in a state of well being and comfort.

An outline of the Standards, which is serving as the framework for the project, was published in the Journal of Medical Education 37: 124-129, 1962. The detailed standards should become available late in 1962.

The Animal Care Panel is planning to use these standards in organizing a voluntary accreditation program for animal facilities. The program will be somewhat similar to the hospital accreditation program of the Joint Commission on Accreditation of Hospitals. The Federation, the Association of American Medical Colleges, the American Heart Association, the Medical Research Association of California, and the New York State Society for Medical Research have issued grants to the Animal Care Panel for this program. Other groups are considering similar support. It is a highly constructive effort which should aid implementation of the Standards.

Legislation

H. R. 1937 (Representative Martha Griffiths, Michigan) and H. R. 3556 (Representative Morgan Moulder, Missouri) are pending in the House of Representatives. Both of these bills would have an adverse

effect on biological and medical research if adopted in their present forms. Copies of the bills are available from the National Society for Medical Research, 111 E. 4th St., Rochester, Minnesota. Proponents of the bills claim that Congressional hearings are imminent. However, as far as can be determined at this time, it is unlikely that hearings will be held during the present Congressional session. Nevertheless, these bills remain a serious threat to the scientific community. They are being advocated by well-organized, well-financed groups. All physiologists should continue to impress legislative people and the general public with the dangerous implications of these bills.

Organizations Supporting Restrictive Legislation

The Animal Welfare Institute (Christine Stevens, President, 22 E. 17th St., New York 3, New York) is the principal supporter of the Griffiths bill. The A.W.I. advocates a system of regulating animal experimentation essentially equivalent to that in England. There has been much discussion recently regarding the attitude of British scientists toward their regulatory system (The Cruelty to Animals Act of 1876). There seems to be little doubt that most research workers in England have learned to live comfortably with the law, and accept it. However, their support or lack of support of the law has no bearing on the suitability of a similar regulatory system for the more massive American research scene. In the judgment of most American scientists the licensing of research workers and institutions and the reporting system for experiments, as proposed in the Griffiths bill, is unnecessary, restrictive, and unwise. The scientific community already is taking definitive steps to assure the best possible care of experimental animals through the Standards program of the Animal Care Panel.

The Humane Society of the United States (1145 - 19th St., NW., Washington, D.C.) is the principal advocate of the Moulder bill. The provisions of this bill are more stringent and onerous than those of the Griffiths bill. The H.S.U.S. has been particularly obnoxious in its activities. It has employed, and is employing undercover agents to gather evidence of cruelty in research laboratories, in support of its campaign for H.R.3556. Tulane University, Stanford University, Loma Linda University, and several other institutions already have been victimized. A striking example of these activities may be found in the book "Animals in a Research Laboratory," published by H.S.U.S. in 1961. Among other things this book contains the "reports" of Thomas Hammond, an H.S.U.S. "investigator" while he was employed as an assistant in the Cardiovascular Laboratory at the White Memorial Hospital (Loma Linda University) in Los Angeles. In view of these activities it would seem prudent for scientific institutions to screen applicants for employment in animal research facilities with great care.

Both the A.W.I. and the H.S.U.S. are conducting aggressive campaigns for public support of their pet bills. Favorable editorials have appeared in a number of local papers. Some branches of the General Federation of Women's Clubs are said to have issued resolutions in support of the bills. The scientific community is not doing enough to inform the public of the true situation. Grass roots activity is needed,

and physiologists should participate. The Committee regards it of particular importance to tell "the story behind the story" of the importance of proper animal care to the conduct of scientific research. Laboratory animal medicine has experienced rapid and dramatic growth as a professional field in recent years. The public should know more about this growth rather than the distorted picture of laboratory practices presented by the H. S. U. S. and A.W.I.

Refresher Course at Fall Meeting

A refresher course on selection, use, and handling of animals for physiological experiments, scheduled for the Fall meeting (1962), has been postponed. This action was taken to permit development of an endocrinology course. Apparently, this is one of the few years that the Laurentian Hormone Conference does not conflict with the Fall meeting; a large attendance by endocrinologists is anticipated. The refresher course in animal care will be rescheduled, probably in 1963.

Additional Legislation

On March 28, 1962, Senator Joseph Clark (Pa.) introduced S 3088. The bill is reported to be the same as the Griffiths bill, essentially identical to the Cooper bill (S 3570) of the last session of Congress. The bill has been sent to the Senate Committee on Labor and Public Welfare (Senator Lester Hill, Chairman). As far as can be determined no hear ings have yet been scheduled.

ANIMAL CARE PANEL MEETING

The Animal Care Panel will hold its annual meeting on October 2-5, 1962 at the Conrad Hilton Hotel in Chicago. Dr. William I. Gay of the National Institutes of Health is program chairman. He plans sessions on:

Germ-free and specific pathogen free animals
Training of laboratory animal caretakers
Laboratory animal diseases
Dog diseases and facilities
Use of farm animals in laboratory work
Laboratory animal facilities
Primates

REPORT OF VISIT TO BIOLOGY DEPARTMENTS

JOHN M. BROOKHART

For the past few years the Council of the Society has asked one of its members to visit several schools of his choice to discuss with their appropriate staff members whatever Society problems seemed to be of importance at the time. I am now reporting on the results of several such visits made during the past winter.

The Council of the Society has been seriously concerned over problems presented by its relationship with regard to physiologists whose major interests lie outside the area which has been roughly described as mammalian, organ, or integrative physiology. There is ample evidence that a growing number of physiologists in this country regard the Society as a group fundamentally oriented toward medical schools with little or no interest in or for general physiologists, zoophysiologists, or comparative physiologists - in short, the physiologists who are most often found working in college and university departments of biology. The need for more specific identification has been expressed in the creation of a Society of General Physiologists and a Biophysical Society. During the past year members of the American Society of Zoologists have initiated exploratory discussions with the Council concerning the possible formation of yet another special group designed to meet the needs of comparative physiologists.

The reactions of the Council to this trend toward greater fragmentation of the Society have been mixed and uncertain. In general, the prospect of schismatic specialization is unpleasant in the sense that it seems to reflect failure on the part of the Society to reach the needs of a substantial proportion (Hardy - The Physiologist, 4, 1961) of its membership. On the other hand, the basic trends in research and education make it increasingly difficult for the Society to be all things to all people interested in processes taking place in living systems. It was in the hope of gaining greater insight into these problems and their possible solutions that I visited several groups of biologists in colleges and universities in the Pacific Coast and Northwest area. I purposely chose institutions in which physiological interests and research were represented in varying degrees of intensity and development. I am delighted to express here my sincere appreciation for the uniformly warm welcome with which my visit was received, for the generous and open hospitality which was afforded me and for the interest and seriousness with which my hosts devoted their valuable time to the discussion of the questions I proposed.

In those departments in which there were staff members with active programs of investigation in physiological processes, I found agreement in the idea that the Society is expressing primarily the interests of physiologists allied with medical schools and that Society activities held little reward for fundamental biologists interested in physiological processes. This reaction seemed to stem from several sources. As might have been predicted, dissatisfaction with Society meetings was expressed. Program content in general and comparative physiological studies were said to be so diluted with mammalian physiological studies as to make the meetings

minimally useful for purposes of self-education. Contacts with other persons for exchange of information and renewal of old friendships started in graduate school were said to be sufficiently rare as to make the meetings minimally useful for this purpose. The use of the Society's journals as avenues of publication was said to be infrequent because of the dilution factor again. In spite of these opinions, those who had already acquired or who were seeking membership in the Society regarded the services to the members and the prestige of membership as sufficient reason for the expenses involved. Feelings of being excluded, "high-hatted," or denied the Society's channels of publication were vigorously denied.

In those departments in which interest in physiology was expressed only through the teaching activities of the department, a feeling of isolation was strongly apparent. Although the publications of the Society were found to be of considerable value in teaching activities, personal contacts with physiologists were strongly desired but lacking. Financial and time requirements were too severe to permit attendance at meetings. Although none of these departments had had experience with the workshop sessions or the visiting professor activities (Mayerson - The Physiologist, 4, 1961) enthusiastic interest in participating in such activities was expressed.

To the reader, who like me, has not had the opportunity to maintain close contact with physiologists in biology departments, these observations may simply sound like the predictable responses of a minority group - both in the sense of numbers and in the sense of interests. It may be argued that the alleged deficiencies of the Society meetings are not real or important, but represent conclusions based upon inadequate sampling. I think it would be a mistake to adopt such a short-sighted view. It is entirely conceivable that physiologists associated with undergraduate biology departments will not always be in numerical minority. In two of the institutions visited, the post-war years have seen a startling growth in physiological investigation, at all levels of organization, carried out by young vigorous staff members with relatively new appointments. In some of the institutions this sort of growth is just beginning and is being encouraged by the departmental administration. In other institutions, the plans for such growth are being vigorously pushed but have not yet been implemented. I was told that this trend is not peculiar to the area visited. The reasons for these developments hinge partly on the growth of the staff and student members which has been going on and will continue plus the recently increased availability of research grant funds for investigations in fundamental biology.

It is my opinion that the Society must very soon determine if and how its activities are to be influenced by these changes which are already taking place. It must decide whether it will make an attempt better to satisfy the needs of a growing population of physiologists having fundamental interests in non-mammalian organisms and processes. Alternatively, it must decide whether to bow to an inevitable development of a separate group organization with specialized and only partially overlapping interests.

In the event that the Society decides to increase its attractiveness to this group of biologists, several suggestions were received as to how this might be accomplished. One suggestion involved the inclusion in the Fall meeting of a special session in the form of a panel discussion or symposium devoted to zoophysiological topics. Such sessions might be organized around a discussion of the comparative aspects of a systemic function; or around the numerous studies of a basic process such as ion transport as it occurs in non-mammalian forms. Such a session would have the double impact of attracting the participation of fundamental biologists in the meeting and informing others of the wealth of species available for use as experimental models. The Fall meeting was identified because of the close temporal relation between the Fall meeting of our Society and the meetings of the AIBS and the Society of General Physiologists, and because it is so rarely possible for biologists to leave their duties at the time of the Federation meeting. Two suggestions had to do with the extension of the Society's activities to non-meeting situations. I have already mentioned the favorable reception given to information about the Visiting Scientist program. It was also suggested that the Society initiate a Visiting Lecture program along lines similar to the program already operated by the Society of Sigma Xi. It was claimed that both of these activities would also have two influences. It was said that any productive investigator who visits a small campus for a short period and discusses his work, and engages in an exchange of views about mutual problems, leaves behind him a ferment of enthusiasm and intellectual stimulation which has encouraging effects upon the staff members and their outlook on research. It was also pointed out that the rewards and the excitement of an academic life in biology is put into a more favorable light in the minds of the students through these kinds of visits.

It may be that the Society will be unwilling or unable to make any organized effort to alter its functions in this regard. The differences between the orientation of undergraduate school and medical school physiologists toward Societies are traditional and, in part, accidental. The frank lack of enthusiasm on the part of premedical students for much of their work in fundamental biology is said to have colored the attitudes of their teachers toward medical school faculty members. To a certain extent and in varying degrees, the people in biology departments are the victims of a cultural lag in the sense that they think that the majority of investigative programs in medical schools are clinically oriented and not sufficiently basic. On the other hand, some medical school physiologists have been known to look with amused superiority upon what they regard as the pointless and impractical efforts of biologists to understand processes taking place in "grubby little beasts." Although the differences are disappearing rapidly, I have been told that biologists have felt a certain degree of resentment because of the more generous amounts of time, facilities and funds available to encourage research in medical schools. It was the opinion of some of those to whom I spoke that these sources of separation cannot be eliminated by any specific action on the part of the Society. It was suggested that continuing evidences of mutual interest and respect fostered by all members of the Society would eventually bring about a closer and more effective exchange of information and viewpoint.

I was most encouraged by the uniform expressions of hope that the American Physiological Society would continue to attempt to represent any and all kinds of physiologists, and that it would not be necessary to form new offshoots made up of specialized groups.

INVITATION TO THE FALL MEETING

The University of Buffalo, Buffalo 14, New York

August 27-31, 1962

The "Buffalo Committee" of the American Physiological Society invites all members, their families and friends interested in physiology to attend the Fourteenth Autumn Meeting of the Society.

The scientific activities will include presentation of papers, symposia, demonstrations and visits to university departments and affiliated research institutions. The Refresher Course in Endocrinology will be conducted under the chairmanship of S. M. McCann, University of Pennsylvania. The Bowditch Lecture will be delivered by T. Hastings Wilson, Harvard University. Other activities scheduled are the Autumn business meeting of the Society, the annual Society banquet followed by the Past-President's address, a reception by the Chancellor of the University of Buffalo, and a picnic excursion to Niagara Falls. The Ladies' Committee is planning several visits of interest, including the Albright-Knox Art Gallery, and is making arrangements for daytime activities for children.

Housing will be provided on the campus in the new university dormitories, and meals will be served on the campus. For those preferring to live outside, several excellent motels are within a very short distance from the university.

Announcements with additional information and the abstract forms are being sent to the membership. The deadline for receiving the abstracts will be June 21, 1962.

We are looking forward to this event and hope to make it a pleasant one.

The Local Committee

THE CONTROL OF ALDOSTERONE SECRETION

JAMES O. DAVIS*

It has been customary at recent Federation meetings for some of the chairmen to review the field with which the specific session is concerned. As I understand it, the purpose of these talks is to provide a background of knowledge for the papers to be presented and to outline the current concepts in the field. There are several areas in which there has been disagreement on the control of aldosterone secretion and an introductory talk on the leading questions in these controversial areas might be helpful.

Long before aldosterone was isolated and identified, it was recognized that a potent sodium-retaining hormone is present in the amorphous fraction of extracts of the adrenal cortex. Similarly, the concept of receptors concerned with the control of the volume of the vascular system originated before aldosterone was discovered. In essays on the pathogenesis of edema in 1948 and 1952, Peters (65, 66) set forth the view that fluid and electrolytes escape from the vascular bed with a resultant decrease in circulating blood volume. In clinical states in which there is an increase in total vascular volume such as congestive heart failure, Peters suggested that a decrease in "effective circulating blood volume" or some function thereof stimulated receptors which he referred to as volume meters or "volumeters." Peters reasoned that these receptors might control the peripheral blood level of the still unidentified sodium-retaining hormone of the adrenal cortex.

In 1950, Deming and Luetscher (20) reported the presence of increased sodium-retaining activity in urine from patients with congestive heart failure. This finding marked the beginning of a new era in our knowledge of the physiology of the adrenal cortex and the relation of the adrenocortical hormones to Na excretion by the kidney. It was soon recognized that this increase in sodium-retaining activity in urine was a reflection of excessive amounts of the naturally occurring hormone, aldosterone. In 1954, the researches of Simpson and associates (73) culminated in the isolation and identification of aldosterone. With the development of methods for analysis of aldosterone in adrenal vein blood and urine, attention was directed to the mechanisms regulating the rate of aldosterone secretion.

In general, studies of the control of aldosterone secretion have been designed to identify the various parts of a receptor-effector system. Two general hypotheses have emerged to explain the regulation of aldosterone secretion. According to the first view (see Fig. 1) there are peripheral nervous receptors possibly in the upper arterial tree or cardiac atria; there is an afferent nervous limb and integration occurs in the central nervous system. A neurohormone or a pineal hormone has been proposed as the efferent limb for such a regulatory system. Proponents

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of the second hypothesis have maintained that a peripheral receptor effects the release of a hormone from a extracranial organ and that this hormone leads (directly or indirectly) to increased aldosterone secretion. The principal difference between the two views is that the central nervous system is not involved according to the latter hypothesis.

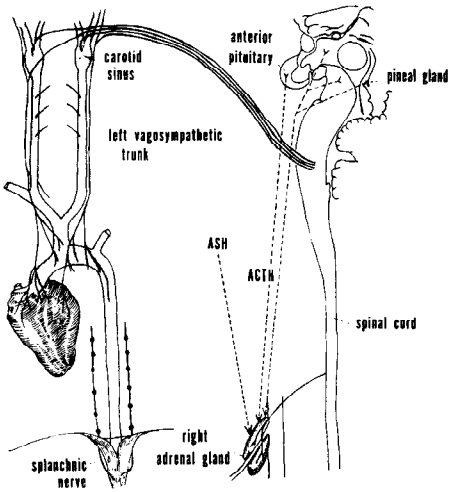

Fig. 1. Diagram of possible nervous afferents, the central nervous system and possible hormones involved in the control of aldosterone secretion. ASH is an abbreviation for aldosterone stimulating hormone. From Davis, J.O. (14).

The evidence for these two hypotheses will be considered in the following order. First, the evidence for the afferent side of the aldosterone regulatory system will be evaluated. Is there a group of peripheral nervous receptors, an afferent nervous limb and a central integrating mechanism? Secondly, what is the immediate stimulus to aldosterone production? What is the role of ACTH, of electrolytes, and of aldosterone stimulating factors in blood, urine and tissue extracts, including extract of the pineal gland and the kidney? Finally, the evidence for the role of the renin-angiotensin system in the control of aldosterone secretion will be presented. This will involve consideration of a receptor-effector system according to the second hypothesis in which the central nervous system plays no essential role.

Possible Nervous Receptors and Nervous Pathways for the Control of Aldosterone Secretion

The original concept of "volume receptors" as proposed by Peters (65, 66) has been supported by many investigators and several extensions of the Peters' hypothesis have been made. Epstein, Post, and McDowell (26, 27) suggested that the renal conservation of Na is conditioned by the degree of filling of some portion of the arterial tree. Epstein and associates (26, 27) cited several situations such as acute hemorrhage in which Na and water retention appeared to be initiated by decreased filling of the arterial part of the circulation. A large body of experimental evidence (1, 2, 11, 13, 27, 29, 53) has accumulated to show that expansion of body fluid volume is associated with a decrease in urinary aldosterone excretion and a natriuresis while contraction of body fluids leads to increased aldosterone output and Na retention. In clinical states with hypervolemia such as congestive heart failure, it has been suggested (11, 13, 27) that the decrease in vascular volume occurs only in the arterial tree or in some local region of the arterial system.

One of the first attempts (1) to examine local regions of the arterial system was concerned with the receptors involved in the moderator reflex. In experimental heart failure, Barger (1) proposed that decreased Na excretion is secondary to a reflex increase in sympathetic activity which originates as a result of a fall in arterial pressure in the carotid sinus and aortic arch. More recently, Farrell and associates (29) suggested that the right atrium acts as a receptor site. They reported that stretching of the right atrial wall decreased aldosterone secretion and on this basis they proposed that decreased atrial stretch augments aldosterone production. Evidence against this hypothesis was presented by Mills and coworkers (56) who found that bilateral cervical vagal section was without effect on aldosterone secretion in intact dogs and that vagotomy failed to block the response in aldosterone secretion to thoracic caval constriction. The consistent finding of hypersecretion of aldosterone in the presence of both a reduced right atrial pressure during acute thoracic caval constriction and a high right atrial pressure in experimental heart failure is also irreconcilable with the right atrial stretch hypothesis.

The common carotid artery and carotid sinus have been proposed as possible loci for receptors controlling aldosterone secretion by Bartter and associates (3). They suggested that alterations in pulse pressure in the common carotid arteries stimulate receptors which initiate a sequence of changes regulating the rate of aldosterone secretion. Carpenter and associates (5) have been unable to confirm the experimental findings reported by Bartter and coworkers (3) for such a receptor mechanism and, in addition, Carpenter, et al. (5) have presented extensive evidence from denervation studies that no such receptor mechanism exists in the upper arterial tree. Also, complete midbrain transection, which interrupts impulses from lower nervous afferents, was completely ineffective in influencing aldosterone secretion and failed to diminish the response in aldosterone production to either acute blood loss or to chronic thoracic caval constriction (15). Finally, decapitation failed to block the response in aldosterone secretion to acute blood loss and the response was no greater in hypophysectomized dogs with the brain intact than in de-

capitated dogs. Collectively, these experiments provide strong evidence against the first hypothesis and suggest that an extracranial organ might function according to the second hypothesis in the control of aldosterone secretion. In other words, a receptor might be located in an extracranial organ and this organ might secrete a hormone which acts on the zona glomerulosa of the adrenal cortex to promote aldosterone secretion.

Role of the Anterior Pituitary in the Control of Aldosterone Secretion

Let us consider the efferent side of the aldosterone regulatory system, that is, the immediate stimulus to aldosterone secretion. Since it is well known that ACTH exerts a profound influence on adrenocortical function, the possible role of ACTH was one of the first factors to be studied in the control of aldosterone secretion. The first evidence to suggest a role of the anterior pituitary in the production of aldosterone was the finding of a fall in aldosterone secretion following hypophysectomy. This result was reported by Singer and Stack-Dunne in rats (74) and by Rauschkolb, Farrell, and Koletsky in dogs (70). Most observers (9, 35, 61, 74) have found an 80-90% fall in aldosterone secretion following acute hypophysectomy; in these early experiments, the animals were subjected to the stress of laparotomy in order to cannulate the adrenolumbar vein for collection of adrenal vein blood. Since stressful stimuli provoked by laparotomy stimulate aldosterone secretion (14), the 80-90% fall in aldosterone production following hypophysectomy occurred from this elevated level secondary to stress. The results of an experiment which shows the decrease in aldosterone secretion which occurs following hypophysectomy of laparotomized dogs are presented in Fig. 2. The average value for aldosterone secretion in ten normal dogs was .024 ug./min. In the hypophysectomized animals, aldosterone secretion was markedly reduced and in five of the animals aldosterone output was less than .005 ug./min.; also, corticosterone production was markedly reduced by hypophysectomy. These experiments demonstrate that loss of anterior pituitary hormones leads to decreased aldosterone secretion and they suggest the possibility that ACTH exerts an influence on aldosterone production.

More recently, the effect of hypophysectomy on steroid secretion has been studied by means of a chronic indwelling catheter in trained, conscious dogs with hyperaldosteronism secondary to thoracic caval constriction (12). Again, an 80-90% fall in aldosterone secretion occurred following hypophysectomy. In hypophysectomized human subjects, a low rate of urinary aldosterone excretion has been found (23, 49, 72) and measurements of the average daily secretion rate by the isotope dilution technique have demonstrated a reduced rate of aldosterone production in hypophysectomized humans (67). It is clear, therefore, that ablation of the anterior pituitary gland is followed by a striking decrease in the rate of aldosterone secretion.

These experiments raise two important questions. First, what specific anterior pituitary hormone or hormones are involved and, secondly, what is the nature of the influence of the anterior pituitary? There is abundant evidence (45, 69) that ACTH exerts an effect on the biosynthesis

of aldosterone. On the contrary, evidence is lacking to show that other anterior pituitary hormones influence aldosterone secretion appreciably. The second question, therefore, is resolved into the nature of the action of ACTH in the biosynthesis or release of aldosterone by the adrenal cortex.

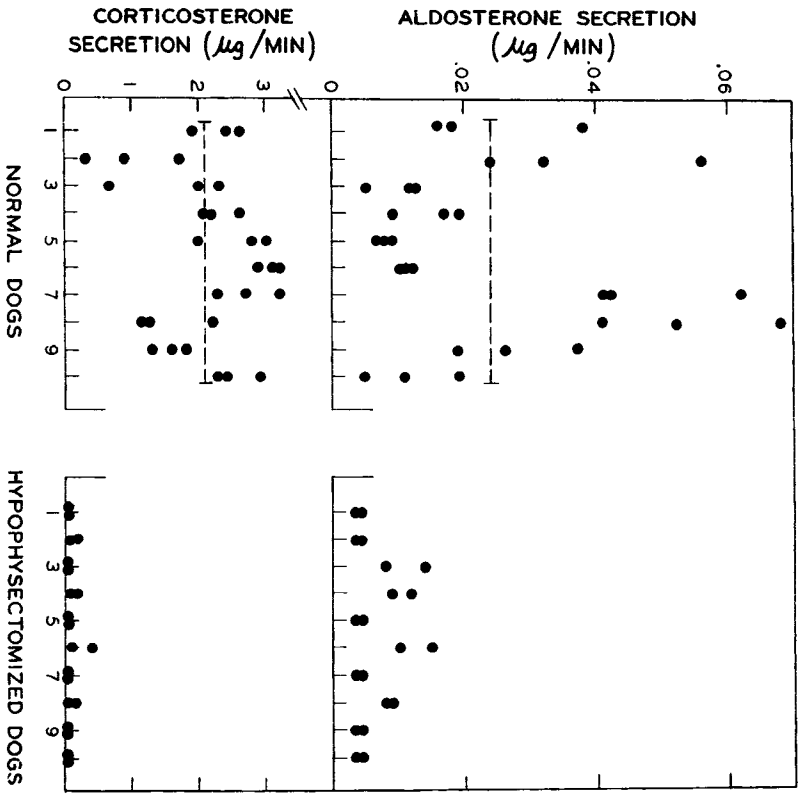

Fig. 2. Aldosterone and corticosterone secretion in 10 normal dogs and in 10 hypophysectomized dogs. Measurements were made in anesthetized animals following laparotomy and cannulation of the right adrenolumbar vein. Hypophysectomy was performed 2 hours before steroid secretion was measured. From Davis, J. O. (14).

It has been suggested (14) that ACTH plays both an initiative and a supportive role in the production of aldosterone. Following laparotomy

(14) and after acute blood loss (7), the striking elevation in the rates of secretion of corticosterone and cortisol suggests the presence of a high plasma level of ACTH. In both experimental situations, the pattern of steroid response is very similar to the increases in aldosterone, corticosterone and cortisol secretion which occur after the intravenous injection of ACTH. Following laparotomy, no mechanism other than increased ACTH release has been described to explain the augmentation in aldosterone output; therefore, in this situation the role of ACTH appears to be an initiative one. After acute blood loss, however, renin as well as ACTH is released (22) so that increased angiotensin II is also present to augment aldosterone secretion. Nevertheless, the greater response to acute blood loss in the intact animal (7, 17, 61) than in the hypophysectomized dog (7, 17, 61) makes it clear that ACTH contributes substantially to the increase in steroid production following acute hemorrhage. It is possible that after acute blood loss, ACTH supports steroidogenesis at a high level and that the action of angiotensin II is the primary mechanism leading to increased aldosterone secretion. The observation that the daily administration of ACTH to human subjects results in a diminution in the response in aldosterone output in urine after 3-5 days of injection of the hormone (53) is consistent with the concept that ACTH is supportive rather than initiative in the regulation of aldosterone secretion.

In experimental secondary hyperaldosteronism, ACTH is very important in the production of aldosterone (9, 12, 14). In this situation, ACTH appears to play a supportive rather than an initiative role. The 80-90% drop in aldosterone secretion which follows hypophysectomy in dogs with hyperaldosteronism secondary to thoracic caval constriction is blocked by intravenous administration of ACTH during the post-hypophysectomy period (Fig. 3). This experiment indicates that ACTH has an important function in the maintenance of the high rate of aldosterone production. On the other hand, studies in conscious dogs with caval constriction and hyperaldosteronism (12) show that only a low plasma level of ACTH is needed for maximal or almost maximal aldosterone secretion. Very high rates of aldosterone secretion were observed in the presence of a low basal output of corticosterone and of cortisol (12), a finding which reflects a low plasma level of ACTH. It seems likely that another mechanism (the renin-angiotensin system) is primarily responsible for the high secretion rate of aldosterone in secondary hyperaldosteronism while ACTH supports steroidogenesis at a high level.

This type of analysis of the functional role of ACTH in the control of aldosterone secretion is a descriptive one which points to our lack of knowledge of the specific steroidogenic action of the hormone. The precise action of ACTH in the biosynthesis of aldosterone as well as the other adrenal steroids is unknown. It has been proposed by Haynes and Berthat (45) that ACTH promotes the formation of reduced triphosphopyridine nucleotide (TPNH) by stimulation of adrenal phosphorylase production. It has been suggested, also, that ACTH is indirectly important for hydroxylation at the 11, 17, 18 and 21 positions since TPNH is required for these reactions (69). The role of ACTH in the biogenesis of aldosterone and the relationship between the effects of ACTH and of angiotensin II in steroidogenesis are among the important unsolved problems

in the physiology and biochemistry of the adrenal cortex.

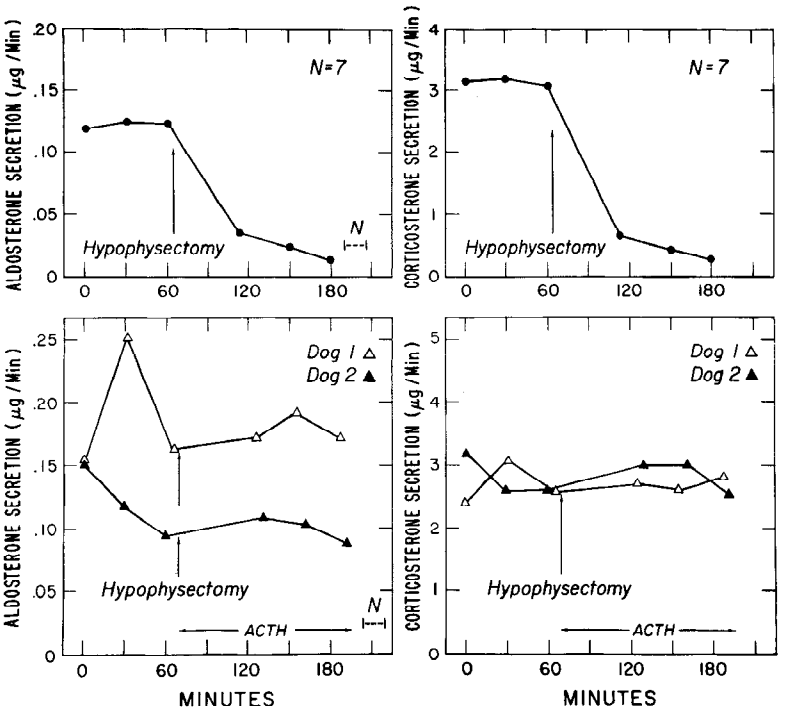

Fig. 3. Effects of hypophysectomy (upper figures) and the blocking effects of ACTH (0.075 units per min.) after hypophysectomy (lower figures) in dogs with thoracic caval constriction and hyperaldosteronism. The average value of 0.024 ug./min. for aldosterone secretion in 10 normal dogs is represented by the dotted line with the N above it in the lower right corners of the figures on the left. All measurements were made in anesthetized, laparotomized animals. From Davis, et al. (9).

Before concluding this section on the anterior pituitary, it should be pointed out that we have considered the efferent system only of the control mechanism mediated by ACTH. It is well established that peripheral stimuli initiate impulses which reach the central nervous system and that this information is relayed to the anterior pituitary. To consider these mechanisms would be to describe the control of ACTH release which is outside the scope of our subject.

Effects of Electrolytes on Aldosterone Secretion

The importance of the Na ion in the control of aldosterone secretion was first reported by Luetscher and Axelrad (54). Since this initial report, it has been repeatedly demonstrated that a low Na intake augments the rate of aldosterone secretion in several mammals including man, and that Na loading decreases aldosterone production. Chronic Na depletion leads to a markedly elevated rate of aldosterone secretion (8, 16) and hypersecretion of aldosterone has been observed in hypophysectomized Na-depleted animals (16). Although ACTH is unnecessary for Na depletion to increase aldosterone production, in the presence of the anterior pituitary ACTH may function to support steroidogenesis at a higher level than in the hypophysectomized animal during chronic Na depletion. The primary mechanism by which Na depletion augments the rate of aldosterone secretion appears to be mediated by the renin-angiotensin system (16, 18) which will be considered later.

In contrast to the unequivocal evidence for the influence of alterations in Na intake on aldosterone secretion, there has been considerable divergence of opinion on the role of K in the control of aldosterone secretion. Several workers (2, 21, 28, 48, 50, 53, 63) have reported that K loading augments the rate of excretion of aldosterone in urine. Some investigators have found this only during a low Na intake while others (2) have reported increased aldosterone output in urine in the presence of a normal intake of Na. Hernando and associates (46) reported that 4 of 5 normal human subjects failed to show an increase in urinary aldosterone output when K loading was superimposed upon a low Na regimen. Rosnagle and coworkers (71) were unable to detect an increase in aldosterone secretion in intact dogs during K loading.

In considering the mechanism of action of K, Laragh and Stoerck (50) proposed that the level of plasma K is the primary determinant of the rate of aldosterone secretion during changes in K intake. Moran and associates (57) reported that elevation of the peripheral plasma level of K by intravenous infusion of KCl in intact dogs augmented aldosterone secretion. On the other hand, Gann and Bartter (34) found no effect of peripheral intravenous infusion of KCl in intact dogs but reported a striking increase in aldosterone secretion during intracarotid arterial injection of K. The Australian workers, Denton, Goding, and Wright (21) reported that a low plasma Na concentration (120-130 mEq./L) and a slightly elevated concentration of plasma K (4.5-5.5 mEq./L) augment aldosterone secretion. In their experiments, blood with altered Na and K concentrations perfused an isolated adrenal in conscious sheep. They suggested that both a drop in the concentration of plasma Na and an increase in the plasma K level were necessary to increase aldosterone output and that an alteration in neither alone was effective.

There are, therefore, several unresolved problems in regard to the role of K in the control of aldosterone secretion. First, there is no unanimity of opinion on the conditions and consistency with which K loading augments aldosterone output. If a high K intake increases aldosterone production, does this occur only in the presence of a low Na intake? Are the effects of Na depletion and K loading mediated by different mechanisms

and are the effects additive? Does an increase in the concentration of plasma K increase aldosterone secretion and, if so, by what mechanism; does the K ion have a direct action on the adrenal cortex? Finally, do changes in K play a role in the physiologic control of aldosterone secretion and is the occasional finding of a high plasma K in clinical states with edema a secondary cause or a consequence of hypersecretion of aldosterone?

Aldosterone Stimulating Factors in Urine, Blood, and Tissue Extracts

Factors present in urine, blood, and extracts of tissues including extracts of the pineal gland and of the kidneys have been reported to augment the rate of aldosterone production. Orti and associates (64) in 1957 described an active agent in urine collected from Na-depleted rats. Mulrow, et al. (58) in 1959 reported the presence of an aldosterone stimulating agent in urine from normal human subjects. Recently, Peterson (68) has presented evidence for a urinary aldosterone stimulating factor which doesn't appear to be angiotensin II. The active agent failed to increase arterial pressure in hypophysectomized rats and direct infusion of an active fraction of the material into the adrenal arterial supply of an isolated transplanted adrenal in sheep increased aldosterone output but had no influence on corticosterone or cortisol secretion. Additional studies are needed to determine the relation of these aldosterone stimulating factors in urine to the specific aldosterone stimulating hormone in peripheral plasma.

There is abundant evidence for a specific aldosterone stimulating hormone, ASH, in peripheral blood. Indirect evidence that the immediate stimulus to aldosterone production is humoral was obtained by stimulation of the isolated, denervated adrenal to secrete increased amounts of aldosterone. It has been demonstrated that the transplanted, denervated adrenal responds to the stimuli of acute blood loss (7), chronic constriction of the thoracic inferior vena cava (7), and chronic Na depletion (21) with an increase in aldosterone secretion. Direct evidence (79) for an ASH was provided by cross circulation of blood from dogs with hyperaldosteronism secondary to thoracic caval constriction through normal isolated adrenals (Fig. 4) with the result that hypersecretion of the isolated adrenals occurred consistently. The adrenals were isolated by the technique of Hilton and associates (47). Control observations were made by circulation of blood from the carotid artery of the normal recipient, through the isolated adrenals and by return of blood to the external jugular vein of the recipient. During cross circulation, peripheral blood from the chronic donor with secondary hyperaldosteronism was circulated from the donor's femoral artery through the isolated adrenals and returned to the femoral vein of the donor. Aldosterone secretion increased in every experiment; the average increase was 129% which was highly significant. As a control experiment, blood from normal dogs was circulated through the isolated adrenals of normal dogs; no consistent changes in aldosterone secretion occurred and the averages of the control and the experimental values were the same. Also, the concentrations of Na and K in plasma perfusing the isolated adrenals were essentially unchanged throughout the control, cross circulation

and recovery periods. These results demonstrate the presence of an aldosterone stimulating agent in peripheral blood of dogs with secondary hyperaldosteronism. Similar cross circulation experiments were performed in conscious sheep by Denton, Goding, and Wright (21) with essentially the same result as reported from studies in the dog. It is clear from these observations (21, 79) and from subsequent reports (14, 16, 17, 18, 36, 38, 62) that this aldosterone stimulating factor in peripheral blood is not ACTH.

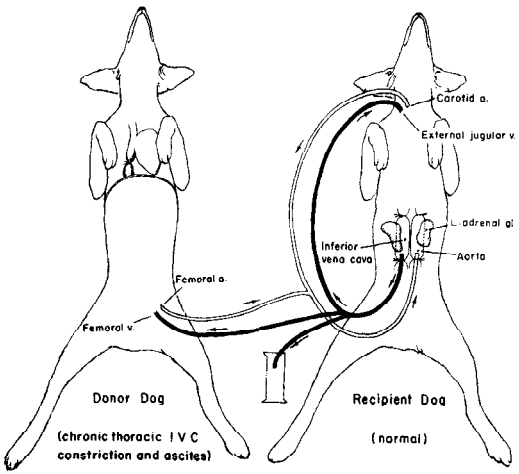

Fig. 4. Experimental arrangement for cross circulation of blood from a donor dog with chronic thoracic caval constriction and ascites (on the left) through the isolated adrenals of a normal recipient animal (on the right). From Yankopoulos, et al. (79).

These experiments which provide evidence for an ASH raise two important questions. First, where is this hormone secreted, and secondly, what is the chemical nature of the substance?

It has been suggested by Farrell and collaborators (29, 31, 32) that the pineal gland or some anatomically closely associated structure secretes an aldosterone stimulating hormone which is a prime regulator of aldosterone secretion. In 1958, Farrell (29) reported that extracts of the pineal gland selectively stimulated aldosterone secretion. More recently, Farrell (32) has presented evidence that the active agent in extracts of pineal tissue has "colorimetric, chromatographic and fluorometric characteristics" identical with 1-methyl-6-methoxy-1, 2, 3, 4-tetrahydro-2-carboline.

Although aldosterone stimulating activity has been reported for ex-

tracts of pineal tissue, ablation of the pineal gland and associated structures including the subcommissural organ, habenular nuclei and posterior commissure has no effect on aldosterone secretion. In a preliminary report, Farrell, Koletsky, and Lapham (30) described a decrease in aldosterone secretion after pinealectomy but, in a later communication, Farrell (31) observed no effect of pinealectomy and an increase in aldosterone secretion occurred secondary to Na depletion in pinealectomized animals. Observers (8, 11) from other laboratories have likewise found that pinealectomy failed to reduce the rate of aldosterone secretion. This finding of no effect of pinealectomy raises the question of the origin of the activity in pineal extracts described by Farrell. Could this activity be attributable to a compound formed from pineal tissue during the extraction process rather than a physiologic substance which is secreted?

In 1960, it was discovered (10, 14, 60) that the kidney is the source of a potent aldosterone stimulating factor. Evidence for this factor was obtained by classic endocrine techniques. Removal of the kidneys in hypophysectomized dogs was followed by a 50% reduction in the rate of aldosterone secretion. The studies were conducted in hypophysectomized dogs because ACTH is released secondary to laparotomy in acute experiments and increased circulating ACTH would prevent the drop in aldosterone secretion following removal of ASH. Application of the stimulus of acute blood loss, which produces a substantial increase in aldosterone production in simple hypophysectomized dogs, failed to augment aldosterone secretion in nephrectomized-hypophysectomized dogs. Injection of saline extracts of each animal's two kidneys effected a striking rise in aldosterone production.

At essentially the same time in 1960, Genest and associates (39, 40) and Laragh and coworkers (51) reported that the intravenous infusion of synthetic angiotensin II increased aldosterone secretion in man. Since these initial reports on the renal aldosterone stimulating factor and on angiotensin II, independent observations (4, 6, 16-18, 36, 38, 52, 59, 62) from several laboratories have provided convincing evidence for the important role of the renin-angiotensin system in the control of aldosterone secretion.

Role of the Kidney in the Control of Aldosterone Secretion

The suggestion of a close functional relationship between the adrenal cortex and the kidney has been made by several workers during the past decade. In 1951, Deane and Masson (19) reported that injection of partially purified solutions of renin produced enlargement of the zona glomerulosa of the adrenal cortex in rats. Hartroft and Hartroft (25, 42-44) have studied the relationship between the juxtaglomerular cells of the kidney and the adrenal zona glomerulosa. They have provided very strong evidence that renin is secreted by the juxtaglomerular cells and that renin has a trophic action on the zona glomerulosa. In 1957, Dunihue (24) found an inverse correlation between the amount of the mineralcorticoid, desoxycorticosterone acetate, which was injected and the degree of granulation of the juxtaglomerular cells in rats. In 1958, Gross (41) postulated a control mechanism for aldosterone secretion which is very close

to our present concept. He suggested that renin via angiotensin II promotes aldosterone secretion and that a negative feedback mechanism operates secondary to Na retention by the kidney with the result that renin release is diminished. In 1959-1960, Tobian (75, 76) formulated a plausible working hypothesis on the nature of the stimulus which leads to release of renin. Tobian (75) found that the degree of juxtaglomerular cell granulation in the kidney was a function of the arterial perfusion pressure. With a high arterial pressure, degranulation of the juxtaglomerular cells occurred whereas the degree of granulation of the juxtaglomerular cells was greater with low perfusion pressures. These findings led Tobian to suggest that a decrease in stretch of the renal afferent arterioles occurred secondary to the decrease in pressure or volume of blood and that this decrease in stretch of the renal arteriolar wall stimulated release of renin by the juxtaglomerular cells. Within a year after the formulation of this hypothesis, actual measurements of aldosterone secretion (10) provided evidence for the role of the kidney in the control of aldosterone secretion.

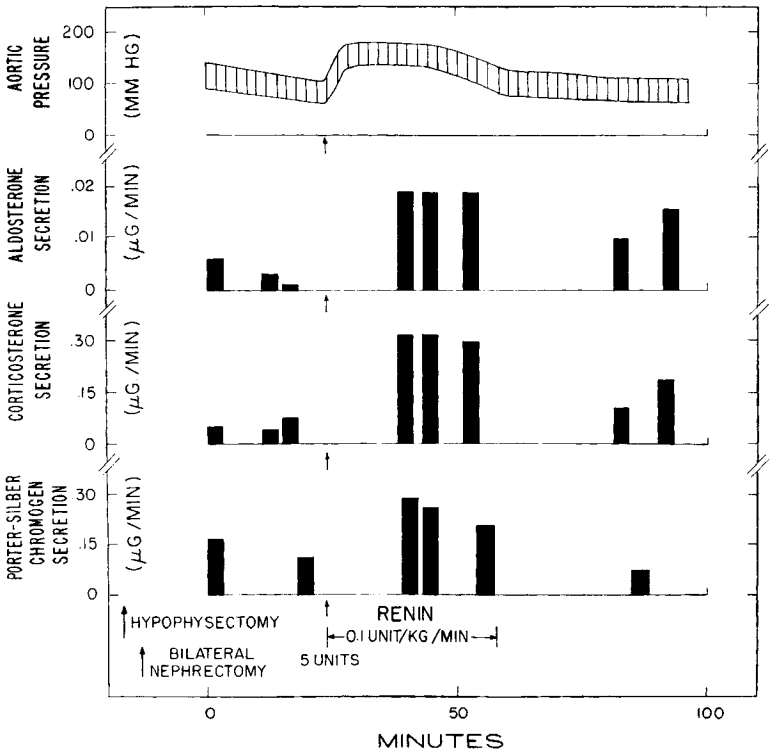

Fig. 5. Effects of intravenous injection of renin on arterial pressure and steroid secretion in a nephrectomized-hypophysectomized dog. From Carpenter, Davis, and Ayers (6).

Several lines of evidence indicate that the aldosterone stimulating factor secreted by the kidney is renin and that the renin-angiotensin system is a prime regulator of aldosterone secretion. First, intravenous infusions of both renin (Fig. 5)(6, 18) and synthetic angiotensin II (6, 39, 40, 51, 59) augment aldosterone secretion. Second, synthetic angiotensin II acts directly on the adrenal cortex; this was demonstrated by the occurrence of a striking increase in aldosterone and corticosterone secretion within 5 min. after the injection of very small amounts of angiotensin II (which were ineffective given systemically) into the arterial supply of isolated adrenals (Fig. 6). Third, the pattern of steroid response to renin and to synthetic angiotensin II is essentially the same as that observed with kidney extracts (6, 16, 18, 62). A striking increase in aldosterone secretion occurred with doses which produced definite increments in corticosterone and cortisol secretion but these latter changes were physiologically insignificant (see Fig. 5 for pattern of response to renin). Also, the steroid response to angiotensin II is distinctly different from that observed with ACTH. Ganong and Mulrow (37) found that low doses of ACTH produced a prominent effect on cortisol output with less influence on aldosterone secretion (Fig. 7). Fourth, fractionation studies of crude kidney extracts (18) have demonstrated that the only fraction with aldosterone stimulating activity was the renin

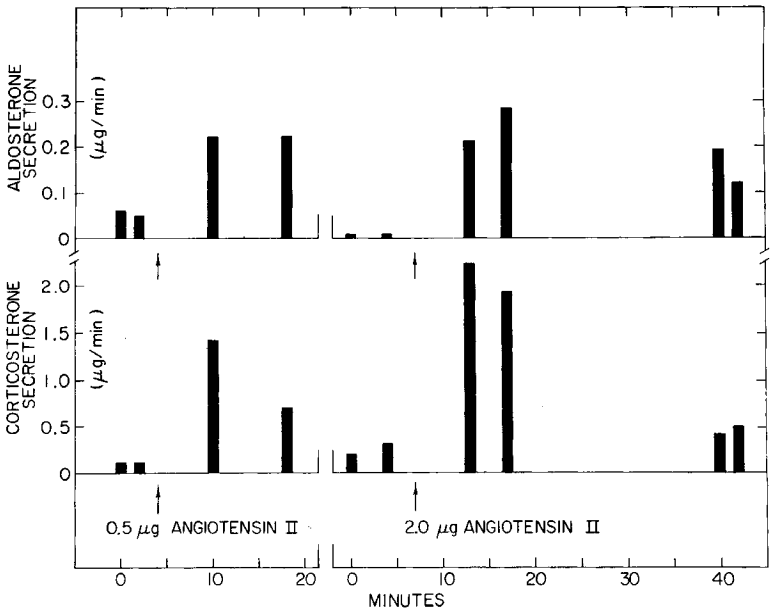

Fig. 6. Effects of injection of synthetic angiotensin II at two dose levels into the arterial supply of isolated adrenals of a nephrectomized-hypophysectomized dog.

fraction. Fifth, in secondary hyperaldosteronism several findings (16, 18, 43, 44, 55, 77) implicate the renin-angiotensin system in the control of aldosterone secretion. Removal of the kidneys in hypophysectomized dogs with hyperaldosteronism secondary to thoracic caval constriction produced a marked fall in aldosterone secretion and extracts of the kidneys from these animals increased aldosterone production (16). The renin content of the kidney is increased in dogs with hyperaldosteronism

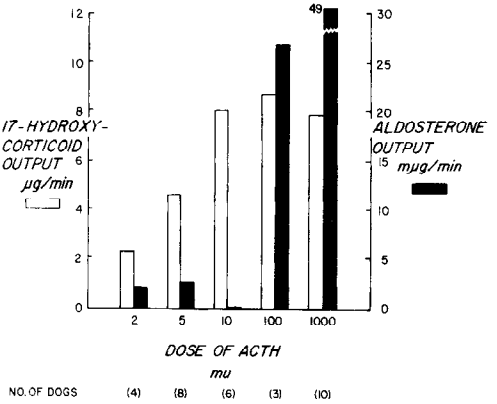

Fig. 7. Effects of ACTH on aldosterone and 17-hydroxycorticoid output in hypophysectomized-nephrectomized dogs. From Ganong, Mulrow, and Cera (37).

secondary to thoracic caval constriction (16) (Fig. 8) and secondary to chronic Na depletion (43). In 1946, Merrill (55) catheterized the renal vein in patients with congestive heart failure and demonstrated a high concentration of renin in renal vein blood. Hyperplasia and hypergranulation of the juxtaglomerular cells have been observed both 1) in experimental hyperaldosteronism secondary to thoracic caval constriction (18) and to chronic Na depletion (43), and 2) in patients with cardiac failure and decompensated hepatic cirrhosis (44). Tobian (77) obtained a high positive correlation between the degree of juxtaglomerular cell granulation and the rate of Na retention in rats with nephrosis produced by aminonucleoside. Sixth, in experimental renal hypertension (6), hypersecretion of aldosterone occurred in dogs with malignant hypertension only and the renin content of the kidney was elevated ten-fold. In contrast, dogs with benign experimental renal hypertension (6), showed a normal rate of aldosterone secretion and the renin content of the kidney was only doubled. Seventh, Edelman and Hartroft (25) have presented new convincing evidence with the fluorescent antibody technique that the juxtaglomerular cells of the kidney are the source of renin. There is, therefore, considerable evidence that the renin-angiotensin system

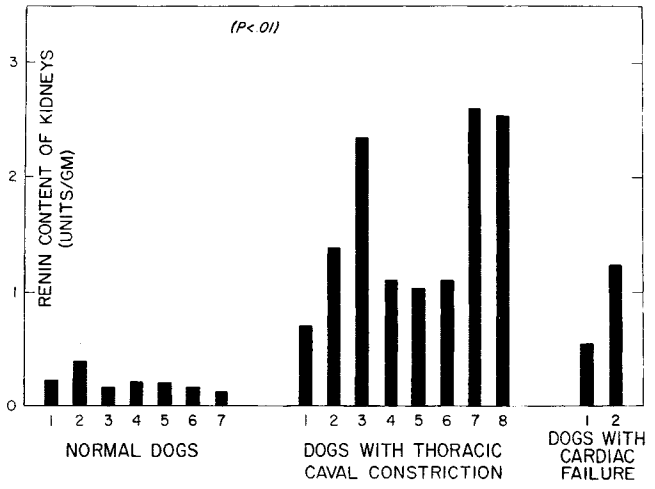

Fig. 8. Renin content of kidneys in a group of normal dogs, dogs with thoracic caval constriction and dogs with experimental heart failure. From Davis, et al. (18).

is the primary mechanism for the control of aldosterone secretion.

It should be emphasized that the slight increases in corticosterone and in cortisol secretion following the injection of large doses of renin or of angiotensin II do not constitute evidence against the importance of the renin-angiotensin system in the control of aldosterone secretion. Also, following acute blood loss or during acute aortic constriction, stimuli of sufficient magnitude to increase aldosterone secretion substantially produced only slight increments in corticosterone secretion. In normal, stressed dogs, the absolute rate of corticosterone secretion (2.34 ug./min.) is 100 times greater than the simultaneous rate of aldosterone production of .024 ug./min. It is clear, therefore, that a substance such as angiotensin II could act at an early stage in the biosynthetic process and by production of a slight amount of corticosterone could provide substrate for a substantial increase in aldosterone output. The finding that corticosterone secretion consistently fell following bilateral nephrectomy of both hypophysectomized dogs with thoracic caval constriction and Na-depleted hypophysectomized dogs (16) agrees with the result that angiotensin II augments corticosterone production.

The precise sequence of changes which occurrs in the regulation

of aldosterone secretion by the kidney is not completely settled. The following scheme is proposed as a plausible working hypothesis (Fig. 9). The principal parts of the renal aldosterone regulatory system are 1) the renal afferent arterioles, 2) the juxtaglomerular cells in the media of the renal afferent arterioles, 3) the renin-angiotensin system, 4) the zona glomerulosa of the adrenal cortex, 5) aldosterone, and 6) the renal tubule cells. According to this view, the renal afferent arterioles constitute the receptor site; these arterioles appear, therefore, to be the elusive so-called "volume receptor" which has been sought for more than a decade. As suggested by Tobian (76, 78), the afferent signal might be provided by a decrease in stretch of the renal afferent arterioles with the resultant release of renin by the juxtaglomerular cells. This hypothesis seems to be the most reasonable one at the present time but

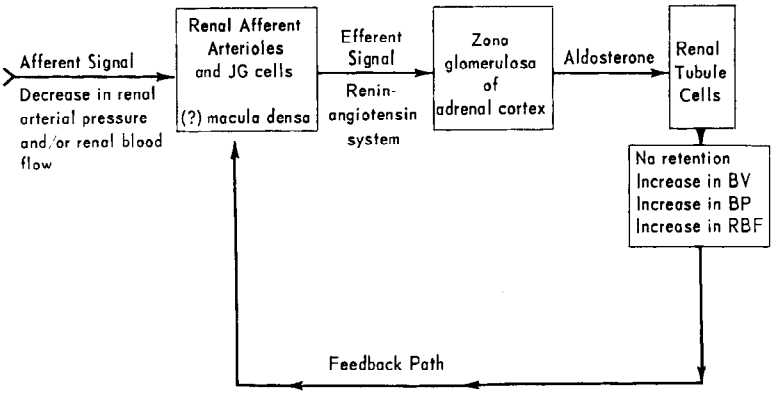

Fig. 9. Proposed scheme for negative feedback mechanism for control of aldosterone secretion.

it leaves unexplained the striking juxtaposition of the macula densa to the juxtaglomerular cells of afferent arteriole. Although this anatomical relationship may have no functional significance, the macula densa could be part of the receptor mechanism. Of possible importance in this connection is the evidence for a close correlation between hexose monophosphate shunt enzymes of the macula densa, the degree of juxtaglomerular granulation and pressor activity in extracts of kidneys of rats with a variety of forms of experimental hypertension (33). Because of the possibility that macula densa is part of the receptor mechanism, it has been included in the proposed scheme (fig. 9). It seems clear that the efferent signal is the renin-angiotensin system and that angiotensin II acts directly on the effector site, the zona glomerulosa of the

adrenal cortex, to increase the secretion of aldosterone. Aldosterone acts on the renal tubule cells to promote Na transport and, thereby, Na retention by the kidney*. Sodium retention is accompanied by retention of water and expansion of the circulating blood volume. According to this concept, the blood pressure and blood flow through vital organs including the kidney are increased. These changes would increase the stretch of the renal afferent arterioles and by this negative feedback mechanism result in decreased release of renin.

Such a control system provides a reasonable basis for the physiological regulation of aldosterone secretion. The effects of alterations in daily Na intake on aldosterone secretion could be mediated by this negative feedback system which would thereby provide one of the primary mechanisms for transient acute changes in the rate of aldosterone secretion. In chronic Na depletion, the evidence (16, 18) clearly indicates that the hyperaldosteronism is mediated by the renin-angiotensin system. It is likely, therefore, that a change in Na intake from one day to the next and the associated alteration in aldosterone secretion are mediated by small changes in blood volume, arterial pressure and renal blood flow and by release of renin. Measurements of the small physiological changes in arterial pressure, renal blood flow and aldosterone secretion are needed to provide more definitive evidence for a normal regulatory role of this mechanism.

In several experimental situations it has been demonstrated that a decrease in renal arterial pressure and in renal blood flow augments aldosterone secretion presumably secondary to release of renin by the juxtaglomerular cells. Following acute hemorrhage, a reduction in pressure and flow through the kidney occurs and aldosterone production is increased. Acute suprarenal aortic constriction (18) reduces renal arterial pressure and renal blood flow and augments aldosterone secretion. In both experimental low and high output heart failure (11, 18), a decrease in blood flow and arterial pressure in the kidney is a consistent finding. These experimental results suggest that some renal functional change, possibly a decrease in stretch of the renal afferent arterioles, leads to release of renin in several experimental states with secondary hyperaldosteronism. It now appears that the functional change associated with an alteration in total vascular volume which Peters (65, 66) referred to as decreased "effective circulating blood volume" is the decrease in the pressure or volume of blood in the renal afferent arterioles. In congestive heart failure, this renal functional alteration stimulates the juxtaglomerular cells to release renin so that chronic hyperaldosteronism, Na retention and hypervolemia result. Arterial pressure and blood flow through the kidney are partially restored. The compensation is, however, inadequate and hypersecretion of renin and of aldosterone lead to an abnormal state with chronic fluid retention and edema.

* It should be pointed out that chronic Na retention is dependent upon an extra-adrenal factor in addition to the high plasma level of aldosterone (11).

Summary

The evidence concerned with mechanisms controlling aldosterone secretion has been reviewed in terms of two current views. Experimental results supporting the hypothesis of cardiac and central arterial nervous receptors, nervous afferents and a central integrating mechanism for the control of aldosterone secretion have been presented. Evidence to the contrary, namely, that neither extensive denervation of the central arterial system and cardiac atria nor decapitation failed to block the mechanisms leading to increased aldosterone secretion was cited. These latter results support the alternative view that an extracranial organ secretes a hormone which provides the immediate stimulus to aldosterone production.

Evidence is presented for such a specific aldosterone stimulating hormone in peripheral plasma. In addition, ACTH is important in the production of aldosterone but the precise role of ACTH in the biosynthesis and release of aldosterone is unknown. The effects of Na and K on aldosterone secretion and the possible mechanisms of action of these ions are discussed.

Current findings favor the view that the primary mechanism for the regulation of aldosterone secretion is the renin-angiotensin system. The mechanism is activated by a renal functional change which occurs secondary to a decrease in renal arterial pressure and renal blood flow. The most plausible hypothesis is that a decrease in stretch of the renal afferent arterioles leads to release of renin by the juxtaglomerular cells. Renin leads to the formation of angiotensin II which acts directly on the zona glomerulosa of the adrenal cortex to increase aldosterone secretion. It appears likely that a negative feedback mechanism operates by way of salt and water retention secondary to an increased blood level of aldosterone, and, as a consequence, an increase in blood volume, arterial pressure and renal blood flow occurs.

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NEWS OF SENIOR PHYSIOLOGISTS

D. B. DILL

In January 1962 the following inquiry was sent to all members of the Society born before 1898.

> "Several inquiries come to our committee each year for senior physiologists willing to take a temporary teaching post. Are you a candidate? If so would you also want research facilities and funds? What proficiency do you have in foreign languages? Two of these inquiries have been from Spanish America. Knowledge of Spanish is desirable but may not be obligatory. Any news items for THE PHYSIOLOGIST?"

By early March there were 120 replies. Of these, 84 werenot interested in accepting a temporary position for various reasons such as health, age or the prospect of continuing for some years in their present position. Twenty manifested interest; the majority are available now, others will not be available before the summer of 1963. Among those who replied, the following notes will be of interest to readers of THE PHYSIOLOGIST.

There is a current trend to continue appointments beyond the customary retirement age. This is true of F. L. Hisaw at Harvard (after June 30), R. C. deBodo at New York University, A. F. Cournand at Bellevue Hospital, H. Roberta Hafkesbring at Women's Medical College, J. L. Johnson at Howard, and Wallace Fenn at Rochester. Dr. Fenn retired as chairman but continued as professor. Many are planning a "second career" as Wilder Penfield puts it, or have launched such a career. They often are able to continue in research with support from Federal agencies, e.g. E. F. Adolph at Rochester and D. B. Dill, "Research Scholar" at Indiana.

Several who are in their eighties replied including Percy Dawson (who is writing his autobiography), Samuel Amberg, Torald Sollman, T. S. Githens, and A. N. Richards. Charles D. Snyder, 91, is well and writes of his warm feeling for Indiana because of the influence Jordan and other Hoosiers had on him as a Stanford student, 1892-1896.

Errett C. Albritton is on the staff of the Division of Research Grants, National Institutes of Health. He remarks that training in physiology can be the basis for interesting activities that are far outside the limits of that field.

William R. Amberson, supported by an NIH grant to the Marine Biological Laboratory, is making good progress on his research on muscle proteins. He has built a new home at Woods Hole.

The successful completion of a fund of $500,000 to enable Harvard University to establish the Herrman Ludwig Blumgart professorship in

medicine was announced on November 27, 1961. The new professorship honors Dr. Blumgart, since 1946 professor of medicine at Harvard and physician-in-chief at the Beth Israel Hospital. Most of the contributors to the Blumgart Professorship Fund were present or former members of the professional staff, employees, friends, and trustees of the Beth Israel Hospital who took this means to express their high esteem and abiding affection for Dr. Blumgart.

Harold Bradley is active in the areas of conservation, wilderness preservation, and population control.

Lester R. Dragstedt is research professor of surgery at the University of Florida.

Ernst Gellhorn has finished, in collaboration with G. N. Loofbourrow, "Emotions and Emotional Disorders. A Neurophysiological Study," to be published by Hoeber.

Harry Goldblatt is director of the Beaumont Memorial Research Laboratories in Cleveland.

Fred R. Griffith is teaching physiology in the D'Youville College, Buffalo.

Frederick Gudernatsch spent several months in Germany in 1959 including three at the University of Giessen where he was given an honorary degree. Among other universities, he visited Munich where in 1906 he had become acquainted with Graham Lusk. In December 1960 he was the victim of a mugging; he was robbed of $250 and injured. When he had nearly recovered he suffered a heart block. He has rallied from this and is busy at his home with translating and bibliographic tasks.

Charlotte Haywood will retire in June and is planning a trip around the world. She wonders if some educational group would like her to investigate physiology teaching in Japan, India, or the Near East.

Walter Miles is scientific director of the U.S. Naval Medical Research Laboratory at the Submarine Base, New London. He suggests making use of the Retired Professors Registry, 1785 Massachusetts Ave., NW., Washington, D.C.

Stuart Mudd is Chief of the microbiological research program at the VA Hospital, Philadelphia.

Samuel Pond is helping with registration and counseling at the University of Hartford and is Dean of liberal arts at DeWitt Hall, a new college in Bristol, Connecticut.

Frank Weymouth, after retirement at Stanford, taught for ten years at the Los Angeles College of Optometry and now has a research appointment in the school of optometry, University of California, Berkeley.

In summary, those who replied look back with satisfaction on their

careers in physiology. After formal retirement few wish to be idle and few are idle.

Your committee will furnish information about candidates to department heads who need help either in teaching or in research.

Committee on Placement of Senior Physiologists:

D. B. Dill, Chairman
E. F. Adolph
W. O. Fenn
E. M. Landis

UNESCO SYMPOSIUM

The UNESCO Advisory Committee on Arid Zone Research has arranged a symposium on Environmental Physiology and Psychology in Arid Conditions to be held in Naini Tal, India, August 27 to September 1, 1962. The program will include the following topics:

Medical climatology of arid zones
Physiological anthropology
Comparative physiology of arid lands
Nutrition and heat
Water and electrolytes
Neurophysiology of heat exposure
Significance of solar radiation in the heat balance
Performance and comfort standards
Psychological aspects of life in hot climates

UNESCO proposes to publish the proceedings of the symposium in its Arid Zone Research series.

For information concerning the scientific organization of the symposium write UNESCO, Dept. of Natural Sciences, Place de Fontenoy, Paris 7e, France.

For information on local arrangements write Mr. J. Swarbrick, UNESCO South Asia Science Cooperation Office, 100 Sundar Nagar, New Delhi, India.

PHYSIOLOGY AFTER THE CIVIL WAR

C. I. REED

The effect of the war on progress in education in physiology was negligible in comparison to other contemporary influences, the most important of which was the growing demand for "practical" instruction in medicine. In New York University medical school this demand finally swept out both John W. Draper and his son John C. Draper, although another son Henry Draper (1837-1882; M.D., NYU, 1858), succeeded to the chair (1866-1872) for a brief period; then he too gave up in disgust and transferred his interest to astronomy in which he became fairly prominent. Until the tenure of Graham Lusk (1866-1932; Ph.D., Munich, 1891), begun in 1898, physiology in this school was undistinguished, in fact, not even taught at times.

Martyn Paine (1794-1877; M.D., Harvard, 1816) was Professor of the Institutes (1841-1859; 1867-1877) and published a Textbook of Physiology which was fairly popular for many years. In the chronological history of the school he is listed as the first pharmacologist. These events illustrate several conflicting trends that were evident in many schools. Physiology was initiated ably and enthusiastically but lost prestige and lived out a drab existence with little or no progress until entirely new influences came into play. The course was often omitted for two to five years, often taught by able clinical men, or less able ones not qualified for any other professorial activity, sometimes limited to a brief three weeks. A curious pedagogical anomaly appeared before the war and afflicted the majority of the schools then in operation for periods up to 25 years. When W. H. Welch attended Yale in 1866, he later reported that the course was given over a period of three months in the freshman year then repeated verbatim in the second year. He also testified that Leonard J. Sanford (1833-1896; M.D., Jefferson, 1854) Professor of Physiology (1863-1876) lectured pedantically from a textbook available to every student, held no conferences or quizzes, conducted no original research, and even seemed a little apologetic about his status in the medical school. The excuse for repetition is clear without further comment.

As mentioned in the previous installment, Oliver Wendell Holmes had returned to Harvard to teach anatomy and physiology in the medical school. The time devoted to physiology was variable but usually brief. That he had a consuming interest in the discipline is clear but it is equally clear that he lacked the technical training to do much investigating. He began to realize his own inadequacy and that prompted him to secure the appointment (1864) of Brown-Sequard as Professor of the Physiology and Pathology of the Nervous System, which position he filled for three years. Two years later Holmes abandoned physiology, dividing duties between Brown-Sequard, who returned to France in 1867, and J. S. Lombard,

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This is the fourth installment on the history of physiology. Refer to the following for previous installments, May 1961, p. 34, November 1961, p. 44, and February 1962, p. 35.

who lectured through 1870. The pedagogical activities of these men were undistinguished, which is surprising in view of the prestige accorded the famous Frenchman. Neither students nor colleagues kept any record of personal acclaim for either one.

Meantime, there was emerging on the Boston scene a young man destined to play a role of decisive importance to American physiology. Henry Pickering Bowditch (1840-1911) was one of five children born to a prosperous merchant and insurance executive. After being graduated from a private school along with Oliver Wendell Holmes, Jr., he entered Harvard College in 1857, finishing in 1861, then enrolled in Lawrence Scientific School to specialize in chemistry and natural history. (He had mounted the skeleton of one of his father's horses which had met death from accident.) His sense of patriotic duty forestalled his educational plans and in November of 1861 he became Second Lieutenant in Company G, Second Battalion, First Massachusetts Cavalry. He was promoted through two grades before being wounded in 1863. Furloughed home,he was honorably discharged the following year as probably incurable. However, he re-enlisted as Captain of the Fifth Massachusetts Cavalry and re-entered active service, resigning in July 1865.

He then took up graduate study under Jeffries Wyman to whom he ever after accredited a decisive influence in his future career. A year later he received the magistral, presenting a thesis entitled "Bromide of Potassium." That was a live subject at that time and the paper was published in the Boston Medical and Surgical Journal, 78:177-184, 1868, the first of 49 original papers making up the total bibliography of this man who was to become one of the most important figures in American physiology. In 1868, he was graduated from Harvard Medical School and, later that summer set out for Paris expecting to work with Brown-Sequard who had returned there the previous year. This move may be credited partly to Wyman's advice. The Frenchman's popularity, however, had already taxed his facilities so that there was no place for the young Yankee. He turned then to Bernard and Ranvier, spending about half of his time with each.

His correspondence during this period reveals a state of indecision as to his future career. He was educated for the practice of medicine and his uncle, Henry Ingersoll Bowditch, was one of the most able and progressive physicians in Boston, facts which probably inhibited his response to a strong attraction to a scientific career since he undertook no original research while in Paris. Also, he was greatly attracted to both Charot and Broca. Then, further, he discounted his own ability to make a living in science. His father strongly urged him to follow his real desires and even gave some assurance of financial backing. Oddly enough, the final influence was the association with a number of other young Americans among them the younger J. C. Warren. Although strongly committed to a clinical career, the latter was genuinely interested in improving not only medical education in America but every phase of scientific education. These topics were often discussed during their more leisure moments.

Another factor, which might seem trivial also proved important in keeping his scientific urge alive, arose from his association with Ranvier.

The latter's informal unscheduled "frog walks" originally intended as excursions into the country to catch frogs for the laboratories finally evolved into very earnest seminar discussions so absorbing that the party frequently returned empty-handed because they had forgotten to catch any frogs. Ranvier was at his best as a teacher on these occasions. A visit by Willy Kühne to Paris enabled Bowditch to meet him and on request, he outlined a course of study, the most important feature of which would be a year with Ludwig in Leipzig where Henry arrived in the fall of 1869 after spending some months with Max Schulze in Bonn. Ludwig, probably the greatest trainer of physiologists, had attracted an international group which included men destined to make physiological history for many years, including Lauder-Brunton, Lankester, Von Cyon, Mosso, Kronecker, and Ustimovitch. He interrupted his study there for a brief period to travel in Italy with relatives, terminating this tour with a month in Munich attending lectures on nutrition by Carl Voit. While in Leipzig he invented the Bowditch clock, a timing device for the new kymographion.

At home, after J. S. Lombard (1838-1897;M.D., Bellevue, 1864) discontinued lecturing on physiology, W. T. Lusk, father of Graham Lusk, was appointed Professor of Physiology and promptly set up a program, the full import of which was not appreciated until his son, in 1912, unearthed and published details not previously given prominence. First he published the results of important researches under the title, "Origin of Diabetes, with some New Experiments on the Glycogenic Function of the Liver," which appeared in the New York Medical Journal, Vol. XI, p. 506. More important were his innovations in the teaching program, organizing and synthesizing old and new information into 43 lectures, each accompanied by demonstrations, only a few of which had previously been used in American schools, chiefly by Dalton. Also, Robert Amory lectured twice weekly on the physiological action of drugs. This was not really an introduction to pharmacology as now taught but an extension of instruction in physiology by the use of drugs in demonstrations.

When Charles W. Eliot, an able young chemist became President of Harvard he immediately set out to activate his own intense interest in improving medical education, adopting as his model the pattern set up by John Morgan more than a century earlier. As always, when extensive reforms are undertaken, conservative reactions were antagonistic. Holmes supported Eliot but Henry J. Bigelow, one of the outstanding progressives fifteen years earlier, led a bitter attack on the new policies, culminating in a scathing address at graduation in 1871. Physiology was a special interest of Eliot's. Noting young Lusk's vigorous program, he arranged to have him appointed as head of a new department of physiology. Lusk, however, having learned that Eliot had previously tried to induce Bowditch to return from Europe a year earlier in order to take the appointment, decided that he was not being treated fairly so he entered a partnership for the practice of obstetrics in New York. The offer from Eliot was received the day after completion of this arrangement. Eliot then turned to Bowditch again. He assumed duties as Assistant Professor of Physiology, until he was promoted to full Professor in 1876. Just before returning home in 1871, Henry married Selma Knauth whom he had met at

Oberammergau a year earlier.

Bowditch's scientific and professional activities have been set out in some detail in a number of publications. His son, Harold Bowditch, however, gave this author many details of his career which modify, to some extent, the conventional picture often rather carelessly passed on from one sketch to another. Though he was a vigorous worker and an unemotional scientist he was not an extensive publisher of original research. Everything he did write was well worth reading and well received among his contemporary colleagues abroad. He was not, as often claimed, the first to introduce laboratory instruction in America. No one person can be so accredited. Various laboratory practices were introduced by different persons at different times and in different places. This is to say that laboratory teaching of physiology evolved from humble ideas over a long period not yet completed. In fact Bowditch himself never taught in an undergraduate laboratory. In 1892 he induced Howell to come on from Michigan for the specific purpose of introducing this method. Before accomplishing his purpose Howell was called back to Hopkins to succeed his former teacher. W. T. Porter was then called in from St. Louis and to him must be given full credit for this mutation in Harvard Medical School. Another important point is that Bowditch did not actively train new physiologists. An impressive list was compiled by Walter Meek for the History of the American Physiological Society comprising those who worked informally with Bowditch during these earlier years. Yet all of them had had training elsewhere, their special interests ranging over the entire scope of experimental biology from psychology to surgery; internists, embryologists, geneticists, all were represented, even a budding bacteriologist in the person of H. C. Ernst who probably prepared the first bacterial culture ever grown in America. Out of all of those who did special work with him only Walter Cannon and Warren P. Lombard followed careers as professional physiologists. Nor did he ever confer a graduate degree. He felt that the more pressing service at that stage was to stimulate scientific study in all related fields on the part of those already grounded in fundamentals. There were no formalities of enrollment or registration. Discussions and individual experimental demonstrations were important features of the gatherings. Here was the atmosphere of Ranvier and Ludwig transplanted to virgin environment. When, after ten years, Bowditch assumed the Deanship of the medical school he was obliged to discontinue participation in these gatherings but the general idea was fostered by Cannon throughout his career.

In retrospect, this man's career is baffling. He was highly respected by colleagues abroad and quickly attained to high priority at home. His interests were gregarious and his activities wholly objective. He did not hesitate to join a psychical research group of dubious character just to learn all he could about the concept, not did he hesitate to withdraw when he became convinced that partisan claims could not be supported. His original work was sound and but little modified by later workers. Perhaps its soundness was related to the limited quantity of the output. Cannon testified to his teacher's extraordinary prescience in anticipating some of the problems arising from the x-ray even though he had had no acquaintance with the physical fundamentals involved. Bowditch was seldom

first in anything, yet his influence was such that, without intent, he often overshadowed those who had preceded him.

Dr. Harold Bowditch has told of his gregarious associations, his social geniality, and general friendliness. His wife was of artistic inclination and a musician of ability whereas her husband thought music just organized noise which he accepted without objection. He maintained physiological fitness but had no interest in athletics or organized sports. Perhaps his most significant contribution to American physiology was the dynamic fertilization which he imparted.

Almost simultaneously with the events recounted another mutation was taking place in almost wholly unfertilized territory. As President of the University of California, Daniel Coit Gilman had done a splendid piece of work in organizing the medical school in that university which brought him to the attention of the trustees of the new fund provided by the Baltimore merchant John Hopkins and he accepted a call there in 1876 to undertake the construction of a new university from entirely new materials. While the medical school did not take form until 1893 Gilman saw the necessity of making fundamental preparations, one large segment of which was the development of human biology. The factors deciding his selection of a man to carry out the task have never been recorded but the selection was fortuitous. While the Harvard roots of modern physiology were nurtured in Ludwig's laboratory those for Hopkins were sprouted from anatomical origins by William Sharpey, transplanted by Michael Foster and Thomas Huxley to H. Newell Martin (1848-1896; D. Sc., London, 1872) and in turn, brought to America by the latter. Probably direct correspondence with his two sponsors prompted his appointment. Martin was enthusiastic, energetic, confident, but modest - just the kind of a man to do the job at hand not only intramurally but in public relations. He immediately activated a graduate program and employed as laboratory assistant Henry Sewall (1855-1936; Ph. D., Hopkins, 1881; M.D., Denver, 1889), paying for his services out of his own pocket to the amount of $250 for the year. Thus Martin was the first physiologist in America to fill a full-time chair of physiology with no medical degree. And so far as known now Sewall was the first person to receive a doctorate in physiology from an American school. Sewall, incidentally, was a grandson of Thomas Sewall who played such an important role in the fostering of physiology in Washington half a century earlier. He was granted an honorary M.D. by the University of Michigan but that received in Denver was bona fide. An interesting sidelight on the cross fertilization of biological specialities occurred when Sewall introduced laboratory instruction in bacteriology and one of his first pupils was a young medical student, F. G. Novy. When later, Sewall decided to complete the medical course himself, his bacteriology teacher was Novy who had recently returned from specialization in that discipline in a continental school.

Since Martin relinquished his position when the medical school was finally opened in 1893 none of his graduate students received medical degrees from Hopkins during his tenure although many of them were granted medical degrees later from other schools and Howell, as well as Sewall, was granted an honorary M.D. by Michigan. William Henry

Howell (1860-1945;Ph.D.,1885) enrolled with Sewall in 1881 and continued in the department until he succeeded Sewall at Michigan in 1889 where he taught both physiology and histology. After one year at Harvard (1892-1893) he returned to Hopkins where he spent the remainder of his life. He relinquished active responsibility for physiology in 1921 but continued as Director of the School of Hygiene to 1931. He had been Dean of the medical school (1899-1911) and in 1916 was made Assistant Director of the School of Hygiene. Besides Sewall and Howell, Martin trained an extraordinary group. Together with those turned out by Howell, they largely dominated the field of physiology in the United States for many years. Dunglison had dropped out about the time Eliot went to Harvard. His successor, James Aitkin Meigs, during his ten years of tenure performed no distinctive service, neither did H. C. Chapman, next in line.

After his return from abroad Weir Mitchell continued to exert an important influence until his death in 1914. Early in the fifties he published a critical resumé of scientific contributions of Americans to physiology which went far to stamp him as a leader in the field although he was twice passed over in favor of much less able men, first for Francis Gurney Smith at Pennsylvania and later for Meigs at Jefferson. Mitchell demonstrated in the face of advice from his associates that one could do high grade scientific work simultaneously with the successful and lucrative practice of medicine. As a trustee of the University of Pennsylvania he stimulated a tremendous amount of research mainly by informal association with students and younger staff members. His war experiences gave him the basis for the promotion of clinical psychiatry which was such a prominent feature of his later career. Lastly, he assisted decisively in the organization of the American Physiological Society which he served as second President for a term of four years.

Smith introduced a teaching laboratory for physiology at Pennsylvania in 1876 and ten years later E. T. Reichert expanded this program with the installation of very durable fixed equipment for student use, much of which was still in operation when he retired in 1920.

The establishment of the Index Catalogue of the Surgeon General's Office was an important adjunct to physiological progress as it was in every field of biology and medicine. The infiltration of new scientific information from abroad was greatly facilitated by improved transportation and by use of the telegraph. While importation of personnel was not a major factor it was certainly a very important one. More important was the education of young men who returned from a tour of European schools to bring back with them the best information, technics, and equipment then available. Often these prodigal sons transmitted their new information to others who applied it more vigorously than the transporters.

In 1869 Edward Rives (1833-1883), then teaching in Cincinnati, for the first time introduced a teaching technic that was to become the starting point for the vast science of communication as it has evolved today. This was the use of transparent photographs held in front of a kerosene lamp to project pictures before a class. This soon developed

into the slide projector, or magic lantern, as it was known popularly. Edison is said to have hatched the idea of a moving projection after seeing an operator moving the slide by hand to simulate motion of the subject. Rives first used this formally to project microscope slides. Rives' colleague Alonzo Thrasher Keyt, independently of Marey, contrived a sphygmomanometer which the Frenchman later acknowledged as superior to his own first model which he then discarded. Thus the Marey tambour, so-called, as used in earlier years was actually the Keyt manometer.

Since the Harvard department attained to autonomy there have been only four department heads in physiology. The same number has served the Hopkins department. In Pennsylvania, since the department began in 1789 under Caspar Wistar, there have been 11 heads. These three schools evidently enjoyed a degree of internal stability which must have been an important factor in maintaining a steady productive program.

The impact of the work of Pasteur and of Darwin was a dynamic influence on every aspect of American life as well as on physiology alone. Another influence of great importance was the growth of biochemistry. Chemical physiology had begun to appear in catalogues of medical schools even before 1870, often replacing the old medical chemistry. As a separate discipline biochemistry began to emerge under the leadership of Victor C. Vaugh at Michigan about the time Martin came to Baltimore. Even more dynamically this discipline took form under the guidance of Russell H. Chittenden at Yale. For another half century physiologists and biochemists clubbed together, worked together, replaced and exchanged with each other. Biochemists were members of the American Physiological Society and served as officers thereof. Yet it would not be correct to say that biochemistry is an outgrowth of physiology. So far as one can determine now the separate branches were equally productive, quantitatively and qualitatively.

In another installment, attention will be directed to some of the individuals and institutions who played less continued, though equally important functions in bringing physiology over the adolescent period of second growth.