OPTIONAL FORM NO. 10
5010-104

UNITED STATES GOVERNMENT

Memorandum

707803

608 (R)

R & D files

TO : R. G. Humphries, Director
Contract Division

DATE: OCT 17 1963

FROM : Herman M. Roth, Director
Research and Development Division

REPOSITORY Oak Ridge Operations Ofc. Records Holding area
COLLECTION Documents 1944-1994
BOX No. B-1-5 Bldg. 2714-H
Cont. AT(40-1)2959
FOLDER Med College of VA 1959-63

SUBJECT: REQUEST FOR CONTRACT ACTION

ORS:JDB

It is requested that you take the necessary steps to process the following described contract action:

1. Nature of Action Requested:

/_/ Selection of New Contractor and/or Negotiation of Contract
Number:
Contractor:

/X/ Modification of Contract
Number: AT-(40-1)-2459
Contractor: Medical College of Virginia
Richmond, Virginia

2. Nature of Services to be Covered by Contract: Research

Title: "The Homotransplantation of Fetal Blood Cells and Tissues in Animals Receiving Fatal Whole Body Radiation"

3. Type of Contract /X/ Lump-Sum /_/ Cost-Type /_/ Other

4. Amount to be Obligated by this Contract Action: $42,656.00

5. Description of Other Changes to be Covered by Contract Action:

Modify contract to provide for the performance of additional research to be completed during the period October 1, 1963 through September 30, 1964. The AEC will support the project in the amount of $42,656 in new funds.

ORS Bushnell 10-17-63

ORB

JSH 10/17/63

CONTRACTS-2459 (VA)

ORB

6. Authority:

Form AEC-481 (Contract Authorization) from C. L. Dunham to S. R. Sapiria dated October 7, 1963

DSharp 10-17-63

W 7073

Herman M. Roth
Herman M. Roth

1034527

MEDICAL COLLEGE OF VIRGINIA CONTRACT NO. AT-(40-1)-2459

APPENDIX "A"

For the Contract Period October 1, 1963 through September 30, 1964.

A-I RESEARCH TO BE PERFORMED BY CONTRACTOR

The Contractor will continue to conduct research on the homotransplantation of fetal blood cells and other tissues into animals which have received fatal doses of ionizing radiation. This research will consist of such approaches as (1) study of the effects of rib-shielding in the case of animals which are receiving doses of radiation which would otherwise be fatal, (2) studies on graft radiation where renal homografts receive sequential doses of radiation after grafting, (3) studies on graft radiation in which sequential renal homograft radiation is utilized in combination with treatment with various drugs, (4) studies on the effects of combination of rib-shielding and homograft radiation, and (5) studies on the irradiation of circulating blood *in vitro* directed at attempts to control immunologically competent cells in the peripheral blood.

A-II APPROXIMATE LEVEL OF RESEARCH EFFORT

(a) Contractor Personnel:

	Approx. % of time
Dr. D. M. Hume - Co-Principal Investigator	35%
Dr. R. H. Egdahl - Co-Principal Investigator	25%
5 Research Associates	47%
7 Research Assistants	61%
Veterinarian	10%
X-Ray Technician	25%
Technician	100%
Animal Attendant	100%
Laboratory Aid	100%

(b) Premises, Facilities, and Materials to be Furnished by the Contractor:

Surgical operating rooms for humans and animals are available in addition to Tissue Culture, Hematology and Chemical Laboratories. All the necessary facilities and equipment are available to conduct research on the homotransplantation of fetal blood cells and tissues in animals receiving fatal whole body radiation. Available facilities include X-ray equipment and a 1000 KVP machine.

A-III ITEMS OF EQUIPMENT TO BE PURCHASED OR FABRICATED BY CONTRACTOR COSTING $500 OR MORE

None

1034528

June 3, 1958

Director of Research
Division of Biology and Medicine
U. S. Atomic Energy Commission
Germantown, Maryland

Dear Sir:

Enclosed is a research proposal, in sextuplet, the title of which is: "The homotransplantation of fetal blood cells and tissues in animals receiving fatal whole-body radiation."

This proposal has been signed by us as Co-Investigators and endorsed by a responsible administrative officer of the Medical College of Virginia and also approved by the Governor of Virginia.

We would greatly appreciate your consideration of this proposal and hope that it will meet with your approval.

Sincerely yours,

David M. Hume

David M. Hume, M.D.
Chairman, Department of Surgery

Richard H. Egdahl

Richard H. Egdahl, M.D., Ph. D.
Director of Surgical Research Laboratories

DMH, RHE:mfk
Enc.

1034529

to

DIVISION OF BIOLOGY AND MEDICINE

U. S. ATOMIC ENERGY COMMISSION

Washington 25, D. C.

1. Title of Project-

The Homotransplantation of Fetal Blood Cells and Tissues in Animals receiving Fatal Whole Body Radiation.

2. The Institution and Department in which the work will be done:

The Medical College of Virginia
Department of Surgery

3. Scientific Background:

The exposure of animals to large doses of total-body radiation results in a characteristic sequence of events which has been termed the Radiation Syndrome. Severe disturbances of the hematopoietic, gastro-intestinal, central nervous and other systems occur. However in the lower dosage ranges, survival appears to be threatened principally by the hematopoietic disorder. There are many articles in the literature concerned with preventing, modifying, or treating the hematopoietic disorder. The work before 1952 is summarized by Jacobsen(1) and it is clear from his data and those of others that definite protection against fatal total body radiation is obtained with such procedures as spleen shielding during radiation, injection of spleen cells, or suspensions of spleen and embryo cells, or bone marrow following radiation. Lorenz(2) and Congdon(3) were outstanding contributors also in these early investigative attempts to modify radiation injury with organ shielding or injection of hematopoietic tissues. Most of the workers at that time favored the concept that such measures acted to decrease mortality as a result of a humoral factor present in the material administered to the radiated animal. Although the repopulation of the hematopoietic sites of the host by donated cells was considered a possibility, it was thought very unlikely. Much recent work has been done which makes it necessary to reconsider the cellular repopulation theory for the protective effect of tissue preparations injected into lethally irradiated animals. In 1956, Ford and co-workers(4) demonstrated survival in CBA mice given 950 r and intravenous cell suspensions from homologous infant mice. Furthermore these workers demonstrated that the marker chromosomes of the donor cells were present for long periods of time following radiation. They also injected some lethally radiated mice with rat bone marrow and found that all peripheral blood cells were of the rat type at 19 days. This was the first reported example where cells of a different species not only survived and divided, but functioned in the new host. Nowell and co-workers(5) have also successfully treated lethally radiated mice with rat bone marrow. At 28 days all the circulating cells were alkaline-phosphate positive, indicating that they were of rat origin. Zaalberg(6) and co-workers have extended the heterologous cell treatment of lethally radiated mice to its ultimate by performing skin grafts from rat-cell donor to the radiated mouse. These animals, more than one year after lethal

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MEDICAL COLLEGE OF VIRGINIA

Richmond 19, Virginia

May 28, 1958

Application to the Atomic Energy Commission for Grant to carry out research in: "The Homotransplantation of Fetal Blood Cells and Tissues in Animals receiving Fatal Whole-Body Radiation."

Name of Institution:
Medical College of Virginia

Address:
1200 E. Broad Street
Richmond 19, Virginia

Name of Department:
Department of Surgery

Address:
Box 786, Medical College of Virginia, Richmond 19, Virginia

Name and Title of Department Head:
David M. Hume, M.D.
Professor, Surgery

Mailing Address:
Box 786, Medical College of Virginia, Richmond 19, Virginia

Name and Title of Financial Officer:
W. F. Tompkins
Comptroller

Mailing Address:
Medical College of Virginia
1200 E. Broad Street
Richmond 19, Virginia

Name and Title of Official
Authorized to sign for Institution:
R. B. Smith, Jr., Ph.D.
President

Mailing Address:
Medical College of Virginia
1200 E. Broad Street
Richmond 19, Virginia

David M. Hume

David M. Hume, M.D., Prof. & Head
Dept. of Surgery

R. B. Smith, Jr., President

W. F. Tompkins, Comptroller

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radiation and intravenous rat bone marrow, were found to have circulating blood cells consisting entirely of rat cells, and had accepted some rat skin heterografts for as long as 151 days. It is felt that the heterologous experiments lend very strong backing to those who claim there is cellular repopulation of the hematopoietic areas. Weyzen(7) has actually demonstrated production of rat serum proteins in irradiated mice protected with rat bone marrow. Although such studies do not conclusively demonstrate that the complete and long term replacement of mouse hematopoietic tissue by rat tissue is the reason for survival of irradiated animals, it is difficult to suggest a logical alternative explanation. Inasmuch as the subject of the present proposal concerns homologous transplantation of potential hematopoietic tissue, no further consideration will be given to the heterologous situation.

In 1955 Main and Prehn(8) demonstrated the survival of skin homografts in mice given fatal body radiation and F-1 hybrids, and the authors postulated that the recipients failed to reject the homografts because their active reticulo-endothelial tissue was of donor origin. Trentin(9) has since confirmed these observations and extended them in a beautiful fashion.

Mitchison,(10) in 1956, demonstrated by use of the "second set" phenomenon that there was colonization of irradiated tissue by transplanted spleen cells. These observations, and more recent ones by Ford(11) and co-workers in which specific marker chromosomes were observed in radiated animals given homologous bone marrow 386 days after radiation, appear to offer striking proof for the persistence and multiplication of homologous cells injected into radiated hosts. Parenthetically, it must be added that this does not necessarily establish the cellular repopulation as the basis for survival in the treated irradiated host. Ellinger's(12) work demonstrating protection with a non-cellular extract, is an example of the type of observation that complicates the problem.

It has become apparent that the use of homologous bone marrow, spleen, and thymus in the treatment of fatal body radiation in mice is not identical to the use of isologous hematopoietic tissue. Trentin (13-14) has described the so called "runt" syndrome, in which the lethally radiated mice given homologous bone marrow survive beyond the expected period for untreated controls but later develop a secondary syndrome characterized by emaciation, lymphoid atrophy, and ultimate death. He postulated that a reaction of the graft against the host was the explanation for this phenomenon. Barnes and co-workers(15) have recently shown that the runt syndrome does not occur in all homologous bone marrow injection experiments. Bone marrow injections between CBA and A strain mice invariably succeed if proper attention is given to details of radiation and cell preparation, whereas wasting disease almost inevitably occurs when CBA and C57BL strains are used. It is very interesting that these incompatabilities between various irradiated mouse strains occur in the same strains in which it was difficult to produce acquired tolerance in the experiments of Billingham, Brent, and Medawar(16). Similar findings have been reported by Uphoff and others.

It appears that sufficient genetic dissimiliarity in the H-2 locus results in a high incidence of late reaction when homologous tissue is given to radiated mice. Makinodan[18] raises objections to the generalized acceptance of a graft versus host reaction, but does not offer a convincing alternative. There appears to be little disagreement that when genetic dissimiliarity exists in certain loci, a high incidence of delayed deaths will occur following the homotransplantation of adult bone marrow.

There would appear to be two ways to overcome this problem. One is through the use of inbred strains that do not demonstrate marked genetic incompatabilities. This would represent an idealized laboratory situation, with little potential clinical application. The other is through the use of tissues which lack the capacity to react against the host. The studies on acquired tolerance by Billingham, Brent and Medawar[16] demonstrate that exposure of the fetus to homologous adult tissue at an early stage in development permits the acceptance by the recipient later on, of additional grafts from the same donor. The use of fetal tissues has therefore been suggested for the treatment of fatally radiated animals, based on the concept of acquired tolerance of the transplanted fetal tissues to the host. If such tissues have adequate hematopoietic potential and yet become tolerant to the host's tissue no late deaths should result. Furthermore, even if, as Makinodin suggests, the late reaction is due to rejection of the graft by the host, there is evidence that fetal tissues possess antigenic immaturity[19] as well as immaturity in immunological capacity. There are, therefore, two reasons to be hopeful concerning the use of fetal tissue in the treatment of fatal body radiation.

In preliminary experiments, Uphoff[20] has demonstrated the prevention of the secondary phase of the irradiation syndrome by the use of fetal hematopoietic tissue following lethal total body irradiation in mice. She had demonstrated a high degree of long term protection in the use of mice strains in which there is usually a high incidence of the runt syndrome. Others have suggested the use of fetal tissues, but few difinitive reports have yet appeared. There is a remarkable paucity in the literature on hematopoietic and reticulo-endothelial properties and potentialities of the various fetal tissues at different times of development.

Pertinent references concerning methods of preservation of hematopoietic tissues and radiation studies in the dog will be mentioned in the next section, along with the outline of our proposal. It seems clear that if further progress is to be made in treatment of the radiation syndrome, and through this, in the transplantation of organs, delayed deaths and the runt syndrome must be prevented. The use of fetal tissues, based on the reasoning outlined above, appears to offer a way to overcome this difficulty. If studies with fetal tissue prove successful in strains of mice which normally have a high incidence of delayed deaths, and in dogs, where it is difficult to get survival following total body radiation, clinical radiation trials with fetal donor tissue will certainly seem much more attractive than they do at present with the use of adult bone marrow. This proposal is concerned with the use of fetal hematopoietic tissues in the treatment of animals given fatal total body radiation.

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4. Scientific Scope of the Proposed Research-

There are four principal objectives of the present proposal. The first is concerned with survival studies following lethal body radiation and the intravenous administration of homologous hematopoietic cells. The second is a study of methods of preservation of fetal tissues using tissue culture and glycerol-freezing techniques. If homologous fetal tissues are ever to be successfully used clinically, there must be adequate methods available for their storage. The third is the transplantation of other tissues and organs following a take of the fetal hematopoietic cells. The fourth is a study of the antigenic effect and antibody producing potentials of human embryonic tissues at various stages in embryonic development.

In the first part of these experiments mice will be used, and later dogs. Most of the background literature on mice experiments has been given, and the authors of this proposal are aware that investigation on the use of fetal tissues and lethal body radiation in mice is being performed by Uphoff, Simonsen, Congdon, and many others at the present time. Our objective is principally concerned with experiments in the mongrel dog, where there is greater genetic dissimilarity than between strains of mice. The work of Ferebee(1) has demonstrated the tremendous difficulty in obtaining survival in fatally radiated dogs treated with homologous bone marrow. A very recent abstract by Thomas and co-workers (2) demonstrates that survival is possible with the use of divided doses of radiation, ACTH, splenectomy, and inbred strains of dogs. In the present experiments the dogs will not be inbred. Rather, it will be considered desirable to have unrelated and genetically dissimilar experimental animals so that greater reliance will be placed on the acquisition of acquired tolerance to the host by transplanted fetal tissues. If successful treatment of the irradiation syndrome in humans is ever to be realized, tremendous genetic dissimiliarity must be accepted as an obstacle to overcome, not sidestep. It appears established as a result of the studies of Alpen and Baum, that autologous bone marrow protects fatally radiated dogs. It remains to be demonstrated whether fetal homologous spleen, bone marrow, or liver will protect fatally radiated dogs, and, if so, which tissue is best, and what state of development is optimal.

In the early mice experiments, inbred strains will be used- both these in which runt syndromme occurs and those in which it is rare. Homologous adult marrow will be obtained from the femurs, placed in balanced salt solution and injected at varying times following LD-90 doses of radiation. Radiation will be delivered by a 1000 KVP GE resonant transformer machine. Preliminary dosimetry will be carried out by Dr. William Ham, as will the actual irradiations with the machine. Later, liver, spleen, thymus, and bone marrow of very early embryos will be added to the list of substances assessed for protective effect. Minimum numbers of cells necessary for protection (if such occurs) will be determined.

In the dog experiments, both single dose and multiple dose lethal body radiation will be given. It seems well established by the work of Ferebee(1) and Thomas that several billion cells are necessary to protect lethally radiated dogs. If fetal tissues are protective, numbers of cells necessary will be determined. Attempts will be made to use the female sex chromosome present in adult dog granulocytes as a marker. This was first described by Davidson and Smith(4) for the leucocyte.

It is not known whether this differential feature is present in fetal tissues. Even if the sex tag is not present in the fetal cells when injected, it may appear at a later date, as the cell matures. Two types of control experiments will be performed. In the first, animals will be radiated and given no cells for protection. In the second, the injected cells will be adult cells from the same organs as those used for the fetal cells. In this manner an assessment of relative efficacy of protection will be obtained.

The second part of these experiments will be concerned with methods of preservation. Two methods will be tested:

1. The glycerol freezing technique developed by Polge and co-workers(5) which appears to be practical for storing bone marrow and hematopoietic cells. Barnes and Loutit(6), using the Polge-Smith-Parks technique, achieved a high percentage of survival with preserved spleens of BBA mice given to fatally radiated CBA mice. Personal communication from Hauschka, Congdon and others indicates that the glycerol freezing technique is adequate for bone marrow preservation if proper attention is given to freezing and thawing details. Billingham(7) has preserved skin for long periods of time with the glycerol freezing technique, and has preserved skin for long periods of time with the glycerol freezing technique, and has achieved normal survival when the skin was transplanted back on to the original animal from which it was removed. It is currently planned to suspend the cells in 15% glycerol in balanced salt solution, to freeze them 1 degree per minute in the critical range from 0 to -35° C, and to store them at -76° C. Other concentrations of glycerol will be tested as well. The viability of the preserved cells will be tested by trypan blue staining and by growing them in tissue culture at various times after freezing. The hematopoietic capabilities of the cells will be tested in irradiated animals.

2. The second method of preservation which will be tested is that of tissue culture. Dr. Robert Marston will culture the fresh fetal tissue, and the hematopoietic ability of the cells will be assayed in irradiated animals. The work of Billen(8) and Miller(9) indicates that hematopoietic elements in tissue culture may be effective in transplantation experiments for periods of time up to 21 days, but little is known about tissue culture of hematopoietic fetal tissues. It is possible that fetal tissues will grow more effectively and for longer periods of time in tissue culture, and this point will be investigated with serial passage.

3. The third phase of these experiments will be the transplantation of other tissues and organs into animals which have survived fatal radiation after the administration of fetal hematopoietic cells, or pari passu with the infusion of the hematopoietic cells. It will be important to find out how soon the injected hematopoietic embryonic cells will achieve enough immunological identity to react against the transplanted tissue, and whether the transplanted tissue will react against the host and/or its newly acquired hematopoietic system. When preserved tissue (such as skin) from the embryo hematopoietic-cell donor is used it should, of course, take and grow without difficulty. When, however, the transplanted tissue or organ has been taken from an unrelated adult it might be expected to react against the host even if transplanted simultaneously with the embryonic hematopoietic cells, and against both host and blood cells if transplanted later. It will probably be necessary, therefore, to irradiate the transplanted organ before placing it in the host. This point is important to establish,

since if this technique is ever to be employed clinically it will probably involve the use of embryonic hematopoietic cells and an adult organ from an unrelated donor.

4. The fourth phase of these experiments will consist of studies of human embryonic tissues at various stages of fetal development. These studies will be carried out in an attempt to determine the following: (1) At what stage in human fetal life is hematopoiesis maximal in liver, spleen, and bone marrow? (2) What are the optimal conditions for the preservation of human fetal hematopoietic tissue? (3) At what embryonic age does tissue antigenicity become great enough to lead to transplant rejection? (4) Are sex markers present in human embryonic blood cells? (5) Will embryonic blood cells persist after injection into the normal adult volunteer? If they are non-antigenic and non-antibody forming they may. It will be assumed that they are non-antigenic up until the age established as non-antigenic for the skin grafts. Preserved hematopoietic cells from the donor of the skin grafts will be used.

One of the unique advantages possessed by the Medical College of Virginia is that there is a continuing supply of fetal tissues at varying times of gestation. Study of the fetal tissues obtained from Caesarian section for therapeutic sterilization are already under way. Fetuses from three to 5½ months of age have been obtained, with preservation of liver, spleen, bone marrow and thymus in tissue culture and by glycerol-freezing. Permanent histologic sections have also been obtained. Cellular elements from both liver and spleen have been growing in tissue culture for over a month at this writing, although there is no assurance that they are hematopoietic. It is intended to continue storage of fetal tissues obtained at different times in pregnancy, with assessment of in-vivo viability characteristics and tissue culture growth characteristics at intervals following glycerol freezing. It is hoped that these studies will supply some of the answers to the problems of human homotransplantation when and if there is adequate experimental evidence in mice and dogs that fetal tissue will insure availability of adequate amounts of tissue at the most advantageous embryologic age when opportunity for its use arises. One of the vital questions to be answered in the first portion of this proposal is the age of fetal tissue most desirable to use in this type of experiment. Inasmuch as there is no data on this point, one must hope that ability to acquire hematopoietic activity matures before adult antigenic or immunological characteristics are present. Although several groups of workers, most of whom have been mentioned in the preceeding sections, are at work on this problem at present, to the best of our knowledge no one has clearly delineated these important points.

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REFERENCES-

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7. Billingham, R. E., The storage of skin, in Preservation and Transplantation of normal tissues, Cib. Found. Symp. 160-174, 1954

8. Billen, D., Recovery of lethally irradiated mice by treatment with bone marrow cells maintained in vitro, Nature, 179: 574-575, 1957

9. Miller, C. L., Recovery from irradiation following the adminstration of cultured tissues, Nature, 178:142,1956

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PLAN OF ACCOMPLISHMENT FOR THE FIRST YEAR'S WORK:

1. Develop suitable techniques for the irradiation of mice and dogs, using the side beam from the GE 1000 KVP X-Ray equipment and determine the ~~the~~ dose-response curves for normal animals.

2. Study fresh, glycerol-frozen, and tissue culture fetal tissues at various ages. In vitro cell viability growth in tissue culture and chromosome marker characteristics will be determined. The use of isologous, glycerol frozen marrow in lethally irradiated mice will be taken as a measure of the efficacy of our techniques of preservation.

3. A human fetal tissue bank, consisting of liver, spleen, thymus, and bone marrow preserved by the glycerol freezing technique will be developed. Determinations of cellular viability by in vitro techniques and tissue culture characteristics will be performed on samplings of these preserved fetal tissues. Studies on antigenicity of human fetal skin, already under way, will be amplified.

4. Mice will be given fatal body radiation and homologous, fresh fetal hematopoietic tissues and survival rates will be determined. Skin grafts will be applied in some cases. Glycerol, frozen, fetal tissues will be given to irradiated mice if fresh fetal tissues prove successful. After preliminary experiments have been concluded it is planned, in the latter part of the year, to treat fatally irradiated dogs with fresh and frozen fetal homologous liver, spleen, and bone marrow.

5. Scientific Personnel

Co-Investigator: David Milford Hume-Professor of Surgery, Chairman of the Department, (will devote 25% of time to this program)
Born [redacted]

Home Address: [redacted]

Medical School Address: Medical College of Virginia, Dept. of Surgery, 1200 E. Broad St., Richmond, Virginia

Married, 4 children, ages 14,12,9,5.

[redacted]

1-1-44	to 6-30-45	Assist in Surgery, Harvard Med. School
7-10-45	to 8-3-46	Mil.Ser.U.S.Navy,Surgeon,Aiea Hts.,Pearl Harbor
10-1-46	to 11-30-47	Assist.Res.Surgeon,P.B.Brig.Hosp.
10-1-46	to 11-30-47	Assist in Surgery,Harvard Med. School
12-1-47	to 6-30-48	Assist in Surgery,Harvard Med. School
12-1-47	to 1-1-48	Assist in Surgery.P.B.Brig.Hosp.
1-1-48	to 1-1-50	Harvey Cushing Fellow in Research,Harv.Med.School
1-1-50	to 2-1-51	Teaching Fellow in Surg.,Harv. Med. School
1-1-50	to 2-1-51	Chief Resident Surgeon,P.B.Brig.Hosp.
2-1-51	to 6-30-53	Instr. in Surg.and Dir.,Lab.for Surg.Research,H.M.S
2-1-51	to 6-30-52	Henry E. Warren Fellow
2-1-51	to 7-1-55	Junior Assoc. in Surg.,P.B.Brig.Hosp.
7-1-52	to 6-30-53	
and 1-1-55	to 9-1-56	Scholar in Cancer Research Amer.Cancer Soc.
7-1-53	to 6-30-55	Assoc. in Surg.Harvard Med. School
6-30-53	to 1-1-55	Naval Med. Research Inst.,Bethesda,Md.(Lt.Com.,USNR
7-1-55	to 9-1-56	Assist. Prof.of Surg.& Dir.Lab.Surg.Res.,H.Med.Sch.
7-1-55	to 9-1-56	Assoc. in Surg. P.B.Brig.Hosp.
9-1-56	to present date:	Professor of Surgery and Chairman of the Dept. of Surgery, Medical College of Virginia.

Certification: American Board of Surgery

Surgical Societies: Amer.Col. of Surgeons;Soc. of Univ. Surgeons; Halsted Surg. Soc.; Surg.Biol Club; Amer.Surg.Assoc.; Southern Surg.Soc.; Va.Surg Soc.; Richmond Surg. Soc.; Boston Surgical Society.

Other Medical or Scientific Societies: American Medical Assoc.; Amer. Assoc. for the Advancement of Science; N.Y. Academy of Science; Soc. for Clin. Inves.; The Endocrine Soc.;The American Soc.for Experimental Path.

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PUBLICATIONS

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