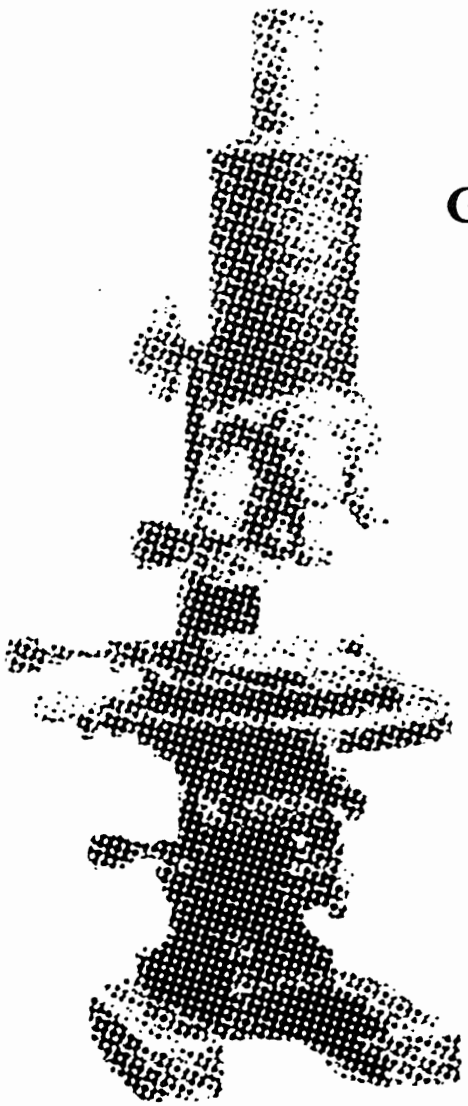
WOMEN IN MEDICINE



Videotaped Profiles
and
Guide For Classroom Use

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Acknowledgements

The **Women In Medicine** project would not have been possible without the cooperative energies of many individuals from the scientific and educational communities. We would like to extend special thanks to key participants in this endeavor.

Videotapes

Jones Gee, Audio Visual Department, Harvard Medical School, who co-produced and directed the WOMEN IN MEDICINE series.

New England Mutual Life Insurance Company and **Harvard Medical School** for co-sponsoring the series.

Guide for Classroom Use

Joy Wallace, Educational consultant, who organized and edited the final version of the Guide.

Jacqueline Bloom, Social Studies Department and **Robert Lockhart,** Science Department, Needham High School who developed questions and lesson plans for the guide after piloting the series in their classrooms in 1983.

James G. Hirsch, M.D., President of the Josiah Macy Jr. Foundation for his personal support of the project and the Macy Foundation for funding the production of the **Guide for Classroom Use.**

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Introduction to WOMEN IN MEDICINE

Background

In 1978, Dr. Linda H. Brink began to research the concept of documenting, in a video format, the contributions of women scientists at the Harvard Medical School.

Using her series **Workers In Tropical Medicine** as a model, Dr. Brink began to work with scientists and historians to explore the various approaches and potential historical and educational uses for this type of oral history documentation. In 1981, Ms. Geri Denterlein joined Dr. Brink in a collaborative effort to research the career patterns of women in academe and they expanded their research to include educators, as well as persons in the fields of high technology and communication.

To produce video material which was visually appealing as well as scientifically and historically credible, Ms. Denterlein and Dr. Brink conducted extensive off-camera interviews and research prior to scripting and shooting the final two to three hour video-taped interview and the two to three hours of on-location footage of the work environment: hospital, laboratory and classrooms. Dr. Brink and Ms. Denterlein edited the series **Women In Medicine** to provide individual 12-15 minute views of the women and to illustrate the many aspects of a successful career in science and medicine.

Purpose

The final video documentation format for the **Women In Medicine** series was selected to fulfill the following aims:

a) provide role models and career information for medical students and junior faculty;

b) encourage young people at all educational levels to consider careers in science and medicine;

c) document, for historians and researchers, the lives and major scientific contributions of women at Harvard Medical School; and

d) increase the visibility of these scientists within the medical community.

Classroom Use

The video series **Women In Medicine** is designed for use in social studies and science classes and in career counseling centers. Nine videotaped profiles introduce students to distinguished women in academic medicine. These tapes may be used individually, in combination, or as an entire series. There are study questions for each tape as well as discussion questions which build upon the entire series or a combination of tapes.

Using these profiles, this **Guide for Classroom Use** develops three main areas of study, each with specific objectives.

General Focus: All students can benefit from examining the primary focus, **Women In Medicine**. Viewed as a whole, the series of interviews enables students to discover patterns in lives and in careers which have implications for men as well as women. Above all, these interviews challenge students to explore careers in medicine and to appreciate the personal qualities and efforts which fostered the productive careers of these nine outstanding women who now become models for others.

Science classes can utilize the interviews as outstanding women in academic medicine discuss some of the basic and important research topics of the day. Although the purpose of the videotapes is not to teach science content, they enable students to discuss the basic scientific principles outlined by these researchers and the issues raised by the impact of scientific discoveries. With some basic knowledge of biology, chemistry and physics, students can explore the scope, significance, and problems of each research discipline presented through the interviews.

Social Studies classes have an opportunity to investigate psychological and social forces which influenced these women in their professional careers as well as the historic struggles which they illustrate. Significant issues rise from the challenges and rewards of pioneering careers.

The format of the **Guide for Classroom Use** includes an introduction to each scientist, a transcript of the video-tape, and discussion questions. Discussion questions are included with social studies, science and general orientations for each scientist. Since the program was designed for such multiple uses, teachers may select the questions which best meet their classroom needs. They may also select among both content questions dealing with specific information from the tapes and from discussion questions requiring a broader examination of the material.

Because the discussion questions should increase interest and raise even more questions, the **Guide for Classroom Use** includes a glossary of key terms and a bibliography to aid further research. Additional supplementary materials include the biographical sketches of each professor, a brief survey of the history of women in medicine in the United States, as well as career information for students interested in medicine.

Additional Teaching Activities

Women In Medicine videotapes lend themselves to a number of additional teaching activities. Suggestions include:

A. Conduct a student survey prior to watching the tapes. Ask about preconceptions regarding careers in medicine, the role of women in medicine and attitudes about science and medicine. After viewing the tapes, readminister the survey to see if any changes have occurred.

B. Invite community women in medical careers to the classroom to speak to students.

C. Take a field trip to a local clinic or hospital to observe and interview people in medical careers.

D. Develop projects that enable students to volunteer in local laboratories, hospitals, clinics and doctors' offices.

E. Assign research projects on topics such as:
- Careers in medicine
- Areas of specialized medicine
- Admissions requirements to medical school
- Relating science experiments to medicine
- Significant medical breakthroughs
- Significant individuals in medicine

Careers In Medicine
Information Packet

The videotapes **Women In Medicine** feature nine women who are senior members of the Harvard Medical School faculty. It may be helpful to have some general background about careers in medicine to fully utilize these tapes.

There were 426,000 physicians in the United States in 1980. These physicians each have at least eight years of post-secondary education, and may have up to 15 years of college education, depending on the specialty.

Entrance into medical school is quite competitive. Between 1981-84, one in approximately 2.5 applicants were admitted to medical school. Figure I shows the total number of medical school graduates in New England in 1979-1980, and the number of minority, female and male graduates.

FIGURE I
New England Medical School Graduates 1979-1980

Medical School	Total Graduates	Minority Graduates	Female Graduates	Male Graduates
CONNECTICUT				
University of Connecticut	84	4	20	64
Yale University	104	12	20	84
MASSACHUSETTS				
Boston University	133	22	55	78
Harvard University	145	34	51	94
University of Massachusetts	96	7	27	69
Tufts University	156	27	47	109
NEW HAMPSHIRE				
Dartmouth University	63	10	21	42
RHODE ISLAND				
Brown University	61	12	25	36
VERMONT				
University of Vermont	70	1	16	54

Source: **Minorities and Women in the Health Field,** 1982 edition, U.S. Dept. of Health.

After completing the coursework for a medical degree, there is generally a one year internship required as well as one year as a medical resident in order to practice medicine. In 1979, the average annual salary of interns and first year residents was about $15,500. All states require that physicians be licensed to practice medicine. To receive a license, a physician must pass an examination and meet the qualifications defined by the state's medical licensing board.

Health Care workers are increasingly in demand and the future job prospects for physicians look favorable.

Physicians frequently work long hours, 55 hours or more, each week and can work irregular hours.

Practicing Physicians can be self-employed, work with partners or be part of hospital staffs. They can work in either the private or the public health sector and income for physicians is influenced by these factors as shown in Figure II.

FIGURE II

Specialty	Median Net Income — 1979 Solo Practitioners	Median Net Income — 1979 Partnerships and Group	Average Annual Income — 1979 Hospital Staff
General Practitioner	$51,770	$69,000	$56,000
Obstetrician/ Gynecologist	$86,000	$92,920	$47,200
Pediatrician	$58,000	$63,130	$49,600
Surgeon	$73,530	$93,330	$52,600

Source: **Medical Economics,** December 8, 1980.

About 8% of all physicians are involved in teaching in medical schools, research or administration. There were 43,337 salaried faculty members in medical schools in 1978. Of that total, 29,960 were white males, 5,681 white females, 3,768 (8.7%) minority male and 928 (2.1%) minority female.

Although there are some women and minority physicians, they are both under-represented. Of the 426,000 total physicians practicing medicine in 1980, 337,000 were white males, 43,000 white females, 32,000 minority males and 14,000 minority females.

There are twenty-two major specialty areas within the medical profession. Almost 2/3 of all physicians practice in the seven largest specialties:

General Practice
Internal Medicine
General Surgery
Psychiatry
Obstetrics and Gynecology
Pediatrics
Anesthesiology

Of these specialties, women are 7.2% of general practitioners, 10.4% of internal medicine, 3.1% general surgery, 17% psychiatry, 11.4% obstetrics/gynecology, 27.3% pediatrics and 14.8% anesthesiology.

The medical specialties shown in **Women In Medicine** include:

pediatrics
anatomy
obstetrics/gynecology
genetics
pathology
microbiology
psychology

These careers are described in the **Dictionary of Occupational Title** in the following way:

Pediatrician: plans and carries out medical care program for children from birth to adolescence to aid in mental and physical growth development.

Anatomist: studies the structure of organisms, separating into parts for detailed study.

Gynecologist: diagnoses and treats diseases and disorders of female genital, urinary and rectal organs.

Obstetrician: treats women during prenatal, natal and postnatal periods; may treat patients for diseases of generative organs.

Geneticist: studies inheritance and variation of characteristics in forms of life; performs experiments to determine laws, mechanisms and environmental factors in origin, transmission and development of inherited traits.

Pathologist: studies the nature, cause and development of diseases and structural and functional changes caused by them; acts as consultant to other medical practitioners.

Microbiologist: studies growth, structure, development and general characteristics of bacteria and other micro-organisms.

Psychologist: investigates problems concerning growth and development of emotional, mental, physical and social aspects of individuals, to increase understandings of origins of behavior and processes of human growth and decline.

Student Handout I

Careers in Medicine

Assignment

Use the **Dictionary of Occupational Titles,** career guidance center materials, college catalogs and the **Careers in Medicine** videotapes, to find the following information.

High school preparation:

List the high school math and science courses a student should take if a career in medicine is contemplated.

Math	Science
_____	_____
_____	_____
_____	_____
_____	_____

Why are these courses recommended for medical school preparation?

Why is it also important for aspiring doctors to also take courses in the humanities?

How are computers currently being utilized in the field of medicine? Why might a prospective medical student want to take a computer class in high school? What computer skills would be useful to learn?

Personal assessment:

List the personality traits required for success as a doctor who deals directly with patient care.

List the personality traits required for success as a doctor who enters medical research.

What experiences can help develop these characteristics?

Which of these personality traits do you have?

List the possible reasons that people could give for entering a medical career.

What interests, hobbies and activites do you like to do that might help you in a medical career?

College preparation:

List the entrance requirements for one medical school.

School: _____

Requirements:

What are the differences between a Ph.D. program and a Med. D. program? Advantages and disadvantages of each:

Ph.D. **M.D.**

Student Handout II

Careers In Medicine

Interview

In order to learn more about a career in medicine, interview a person who has a career in medicine to find the following information:

Name _____

Job Title _____

Job Preparation:

High School —

College —

Graduate School —

Why did you enter this career?

What do you find most satisfying about this career?

What do you find most frustrating about this career?

What advice would you give to someone entering this career?

Student Handout III
Careers In Medicine
Questions

Based on the Careers In Medicine information packet and the videotapes, **Women In Medicine**, answer the following questions:

1. Would you consider a medical career? Why or why not?

2. Why did the **Women In Medicine** choose careers in academic medicine? What similarities and differences appear?

3. Identify the traits that characterize these women. Compare and contrast two of them. What traits do you admire?

4. In what specialties have these women established their careers? What specialties are women entering today? What factors can influence an individual to choose a particular specialty?

5. What were societal attitudes toward women when each of these doctors entered medicine? How have these attitudes changes since then? Why have these changes in attitude occurred?

6. What dilemmas confront men and women who choose a career in medicine? Consider time management problems, as they relate to the integration of family, social life, personal interests and the demands of a successful career.

7. Explain how these women and their careers touched your life.

8. Describe the role models these women give you, personally and professionally, and how they may influence you.

9. How have stereotypes and discrimination limited access for some groups to careers in medicine?

10. Why do you think the number of health care careers is increasing today and there is continued growth anticipated?

WOMEN IN MEDICINE

including biographical information,
video transcript, definition of terms
and discussion questions

I. Mary Ellen Avery, M.D.
II. Elizabeth Hay, M.D.
III. Janet McArthur, M.D.
IV. Ruth Sager, Ph.D.
V. Lynne Reid, M.D.
VI. Alice Huang, Ph.D.
VII. Margaret Brenman-Gibson, Ph.D.
VIII. Shirley Driscoll, M.D.
IX. Priscilla Schaffer, Ph.D.

Profile #1
MARY ELLEN AVERY, M.D.
Professor of Pediatrics

BIOGRAPHY

Dr. Avery, Physician-in-Chief of Boston's Children's Hospital, discusses her research into the respiratory problems of premature babies and her discovery that male infants are at a greater risk than female infants. She describes her role as teacher and mentor to medical students, interns and residents, and recalls that when she was young, a female pediatrician encouraged her to be a doctor. Dr. Avery's commitment to demystify medicine prompted her latest book **Born Early**, which outlines for parents the various treatments and procedures used to save their premature babies.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Pediatricians — (M.D.s) — interns, residents and attending physicians

Medical Students

Nurses

Research Scientists — (Ph.D.s)

Technicians

Medical Equipment Demonstrated:

Incubators, Respirators and Monitoring Equipment used in the Intensive Care Nursery

Social Concepts Discussed:

The Significance of Role Models

The Effect of the Women's Movement on Aspirations and Expectations

Decisions and Factors Affecting Career Advancement

The Importance of Collaboration in Scientific Research

Transcript:

Interviewer: You enjoyed your clinical experience, you loved dealing with patients. Why leave all that and go into the lab? Why pursue research?

Dr. Avery: There's really one compelling reason. It's the frustration of not being able to do enough for patients. It's to watch babies just fade away and die when they were born early, it was to watch them have terrible difficulty breathing and not know how to help them. It's ultimately the awareness of ignorance of what you can do that produces a kind of frustration that produces motivation, part of it's anger — anger that you don't know more and can't help.

Interviewer: The Joint Committee on the Status of Women has created and produced this series on women in medicine with senior women professors at Harvard Medical School. Today we're talking with Dr. Mary Ellen Avery, Thomas Morgan Rotch Professor of Pediatrics, and physician-in-chief at Children's Hospital Medical Center.

Interviewer: Immediately prior to your coming to Children's Hospital Medical Center, you were at McGill, a position you liked very much. What were the enticements to come to Children's Hospital Medical Center?

Dr. Avery: I, of course, had been here from 1957-1959 and knew Boston, Harvard and the Boston Lying-In, as it was then called, had some association with Children's. So the first enticement was old friends and pleasant memories and proximity to my own college, Wheaton College, with more friends from that connection, so that it wasn't coming to a strange area. It was coming home in a way, home and yet a more personal way, a summer home in Maine, which could be reached from Montreal as well as Boston, but it was a consideration in coming to Boston instead of the west coast. I'm comfortable in New England. I like this part of the world, but of course, overriding all of this is that Children's Hospital is a pretty remarkable place. I think it is the preeminent Children's Hospital in the world today and the challenge of leading the Department of Pediatrics in such an institution was one that would be hard to resist!

Interviewer: Before we get into a discussion of your research, I'd like to talk about your personal development and of course the most basic question is, why did you become a doctor?

Dr. Avery: I don't think at this age one ever understands that. The question is often asked; the answers depend on the audience to some extent. I can tell you when — that's pretty clear. That was back in about seventh grade, way back in junior high school. I know that I was heavily influenced by my next door neighbor, Dr. Emily Bacon, who was a pediatrician. She actually showed me my first premature baby at that stage in my life, and it made a lasting impression.

Interviewer: Did Dr. Bacon actively encourage you to pursue medicine?

Dr. Avery: Oh, I think she did, subtly, by virtue of her enjoying her role so much. She loved it and this enthusiasm of hers was contagious. I don't think she said "You should go to medical school" but I think I was aware that she was getting an enormous satisfaction out of life and I guess that I thought that might be something that I'd find satisfying, too.

Interviewer: When you chose medical schools, did you apply to quite a number, or did you just choose Johns Hopkins because you liked it?

Dr. Avery: No, I applied to three, I think. I applied to Harvard, Columbia and to Johns Hopkins and Johns Hopkins accepted me first.

Interviewer: And you wanted to go to Johns Hopkins?

Dr. Avery: Yes, partly because Emily Bacon had gone there. And partly because Johns Hopkins had a reputation for caring about women in medicine.

Interviewer: Can you get into why you chose pediatrics? Was there a course in medical school that particularly appealed to you?

Dr. Avery: No, as a matter of fact, I suppose it was the worse taught course at Hopkins. It certainly wasn't anything that Hopkins did that lured me into pediatrics. It was probably somewhat of a distaste for internal medicine (that's a kind of negative reason) but working with the aged who had many problems that seemed to me not solvable by medicine was something that I didn't find as exciting as working with a younger age group where what you do might have a 70 year payoff and I got excited by preventive medicine. I like to keep people well. Pediatrics is the practice of preventive medicine.

Interviewer: Now on to your involvement with research. You enjoyed your clinical experience, you loved dealing with patients. Why leave all that and go into the lab? Why pursue research?

Dr. Avery: There's really one compelling reason — it's the frustration of not being able to do enough for patients. It's to watch babies just fade away and die when they were born early, it was to watch them have terrible difficulty breathing and not know how to help them. It's ultimately the awareness of ignorance of what you can do that produces a kind of frustration that produces motivation, part of it's anger — anger that you don't know more and can't help.

Interviewer: Along those lines, what are your current research interests and how did they grow out of those initial stages of working with newborns?

Dr. Avery: Well, we're exploring the hormonal regulation of lung maturation. We're pursuing and finding some exciting information about why the male infant is at such a disadvantage compared to the female with respect to susceptibility to a number of pulmonary problems and infections as well. The male/female difference has been known from time immemorial but it's only now that with the help of some pretty talented colleagues, like Dr. Barry Smith and Dr. John Corday, that we're beginning to unravel that question. I think that what's more crucial is my own sense of satisfaction in my research career and the good fortune I've had to excite other people to work in similar areas. I think the greatest reward is my trainees — seeing what they've been able to do.

Interviewer: Let's talk a little about the teaching side of your day. Do you deal with residents quite a bit?

Dr. Avery: Oh, extensively, yes.

Interviewer: In what ways?

Dr. Avery: Well, the house staff is on the front lines of patient care — they ultimately make the decisions that affect the patient most directly. They're the only people who write orders in the order book, for example. So if you care about the quality of patient care, you must care about the house staff. So being involved with the house staff is probably one of my most major functions. I do it through a lot of delegation of course — it's not only my input, it's the whole department's input. But I meet regularly with the chief residents, at least weekly or more often. I meet regularly with the senior residents, again at least weekly throughout the year, and hear from them what's on their minds, hear from them about their problem patients, about any difficulties they're having with other services, for example. Once in a while the surgeons make pediatricians a little mad and tempers can flare on both sides and there is a certain role of peacemaking that comes to me. But largely, it's making sure that the residents know that somebody cares about what they're doing and knows them personally and can provide them with, more often, positive feedback than criticism.

Interviewer: Can you describe your typical day as administrator, teacher and researcher at Children's Hospital?

Dr. Avery: There's no such thing. Maybe that's one of the pleasures of the job. No two days would be more different than two of my days. The proportion of time teaching fluctuates with assignments on the wards where it could be rather extensive. Medical student lectures sporadically throughout the year, not on a continuing basis. The administrative assignments also fluctuate. There is something called "prepare the budget season" which takes on more administrative input than the summer season would, for example. The committee assignments have a way of heating up and cooling down. There are sometimes some big decisions to be made that take a lot of consultation, a lot of administrative time.

Interviewer: Coming through the ranks there are certain hurdles you have to jump to get promoted to the next step, etc. How consciously did you plan these jumps in your own career?

Dr. Avery: I was very aware of them, and I certainly would have been badly put out if they hadn't come at the right time. It's very obvious. You can see what other people are doing. You know what's required to be promoted. This is a part of the small talk of life. The necessity to publish is very evident to anybody and anybody who doesn't do it is not producing the product of scholarship and so even as a house officer I was doing some clinical research. I think I published four papers during my residency years that were built around pursuing ideas that were stimulated by patients, expanding it, talking to people, and finally publishing. I rather enjoyed that. I enjoyed it, but also knew that it was the ticket to academic advancement and the other step — going into the laboratory — was also a ticket; that doing research, gaining independence as an investigator, the ability to bring in grant support, establishing your name in the field, going to meetings, talking, speaking up, it's perfectly obvious what's required in academe. I'm always amazed when someone tells me they don't know what's required. All I can say is where have you been? Open you eyes and look around.

Interviewer: You're also working on a book, which I think you define as part of your leisure time as well because it's a book for the lay public. Could you describe that project?

Dr. Avery: There's been a very dramatic change in the care of small infants over the last decade. It's called neonatal intensive care. It's been written about in a lot of the lay magazines. You can imagine that when a mother has a baby who is then transported to an intensive care environment with lots of high technology, machinery, flashing lights, people running around, the baby seems to be suddenly a piece of the equipment and not a baby. This can be very alarming to parents. Also if they read about the outcome of premature birth in any book that isn't written before the last five years, they'll get the wrong signals. They'll be told of all the problems and they won't know of the successes. We want to humanize that experience. We want to involve parents and we want to explain to them what's going on. They need to know why we do what we do. Now we can spend a lot of time one-on-one explaining that but that takes a lot of time. I wanted something that would be an amplifier to my time — something that the parents could read that would be written in the same tone that I would talk to them. They would ask me questions and I would answer. This is being done with the help of a splendid photographer named Georgia Litwak who photographed all of the equipment and the baby. So we have one baby growing old in time. Instead of a cross-sectional view of lots of babies, we're tracking one and as she grows and develops, Georgia gets her picture and I explain what she's doing and why she's doing it and what we're doing and why we're doing it in laymen's terms. It's a lot of fun!!!

Interviewer: In looking at your life, I can't help but wonder how you've coped with the times when things weren't going so well, and what advice you'd give to people, and what people could learn from your life in a total way, rather than just looking at the climb of your career.

Dr. Avery: I don't know. That's a pretty complicated and sweeping question. Hanging in there is key, I think. Knowing what you want to do and not being easily discouraged is key, particularly in research. You're always moving into the unknown and you can spend months trying to prove something only to find that you made terrible mistakes. You have to be willing to say six months of my life and my hard work went down the drain. And you have to start over. That's terrible discouragement. You can either quit or say I will start over. If it's a question that's worth pursuing, it's probably worth continuing to pursue. The question when to hang in with persistence, perseverance and hard work, when to quit, or when to change course, of course, is a complicated decision, but I think that in the area of scholarly activities one has to have an enormous amount of perseverance. That's key.

Dr. Mary Ellen Avery
Vocabulary

hormonal regulation. Control of the function or development of an organ within the body by specific hormones; e.g. in the male: testosterone slows the development of the lungs.

intensive care unit. Either nursery or surgical ward with advanced technology and specially trained staff to monitor critically ill patients.

lung maturation. Lung development of the fetus/baby prior to birth.

neonatology. Concerned with the medical care of infants from term birth to four weeks of age; often used for the care of premature babies.

resident. Physician who has completed medical school and internship; the residency period can be from one to four years depending on the medical specialty — a "Chief Resident" is usually in the last year of training, and assumes responsibility for all the physicians and medical students below this level.

Dr. Mary Ellen Avery
General Questions

1. Why did Dr. Avery become a doctor? a pediatrician?

2. How early did an interest in medicine emerge?

3. What does Dr. Avery find rewarding and satisfying about her career? Has her career fulfilled the enticements that drew her into her career choice?

4. What hurdles had to be jumped to gain promotion through the ranks?

5. What advice does she give for coping with obstacles and finding success?

6. Who was the individual that was so influential, in her decision to enter a medical career? What other event, in her adolescent years, had an impact on her decisions to pursue a career in medicine?

7. What are the personality traits illustrated by Dr. Avery which are essential for a career in academic medicine?

Dr. Mary Ellen Avery
Science Questions

1. What were the forces involved with Dr. Avery's decision to leave clinical practice and enter the research lab?

2. List the responsibilities of a pediatric physician. What are the responsibilities of an individual doing research in pediatric medicine?

3. What is the current research area that Dr. Avery is involved with? What are some of the new findings in this area of research?

4. What are the other responsibilities of Dr. Avery at the Children's Hospital, besides research?

5. Dr. Avery is writing a book. What is the name of this book and what purpose will it serve? Why is there a need for this type of book?

6. What is the relationship between medical research and the practicing physician, with direct patient contact? Why is this link so essential?

7. The ability to pursue complex research issues is dependent upon a number of traits. What do you feel are the most important characteristics of a successful researcher?

8. Dr. Avery's current research involves an investigation of influencing factors on lung maturation. What factors can influence lung development? From what embryonic tissues do the lungs develop? What ultimately controls lung morphogenesis? Can you propose a model that might explain how some exogenous or endogenous chemical compound could initiate abnormal lung morphogenesis in the fetus?

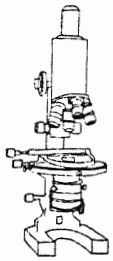
9. How would you define preventive medicine? Does your definition align itself with Dr. Avery's?

Dr. Mary Ellen Avery
Social Studies Questions

1. Describe the development of Dr. Avery's career and the influence of role models, mentors and support systems.

2. What influence did Dr. Avery experience from any of the five sociological institutions (education, family, religion, economic or political)?

3. What assumptions about traditional roles for males and females are challenged by Dr. Avery's experience? What issues are raised or implied?



Profile #2
ELIZABETH HAY, M.D.
Professor of Embryology

BIOGRAPHY

Dr. Hay, Chair of the Department of Anatomy, explains how she combines administrative and teaching responsibilities with her laboratory research in developmental biology. A pioneer in the field of electron microscopy, Dr. Hay recalls the excitement of those early years: "Everything I looked at had never been seen before!" Dr. Hay comments on her experiences at Smith College and Johns Hopkins Medical School, and encourages students to seek the new frontiers of science.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Embryologists

Research Scientists — (Ph.D.s) — post-Doctoral Fellows

Ph.D. Students

Laboratory Technicians

Medical Equipment Demonstrated:

Electron Microscope

Positive Flow Hoods for Sterile Tissue Culture Procedures

Tissue Culture Apparatus

Social Concepts Discussed:

The Effects of the Women's Movement on Aspirations and Expectations

The Importance of Collaboration in Scientific Research

The Changes in Government Funding of Research

Being a Pioneer in Your Field

Transcript

Dr. Hay: You asked me about attitudes of other women. I must say this, when I graduated from Smith, I would say the bulk of my friends thought I was really a little crazy to be going to medical school. They all went out and worked for a year or two and their primary goal in life was to get married.

Interviewer: The Joint Committee on the Status of Women in conjunction with the Office for Educational Programs, has produced this series called Women in Medicine to document senior women of Harvard Medical School. Today we're talking with Dr. Elizabeth Hay, Louise Foote Pfeiffer Professor of Embryology and Chair of the Department of Anatomy.

Interviewer: Can you tell us again, briefly, what electron microscopy meant to your career?

Dr. Hay: Well, it was really the starting point of my career. It was a new technique which promised to open up a whole arena of new information about the structure and function of cells and so when Keith Porter and then with his collaborator Palade in the early 1950's showed that the basophilic substance of the cytoplasm consisted of what we then called Palade granules and are now called ribosomes, attached to membranes of the endoplasmic reticulum. This was just an unbelievable discovery that I heard Keith Porter talk about in 1954 at Atlantic City at a Federation meeting. That was when I decided that this was really for me.

So I went back to Hopkins and struggled trying to learn electron microscopy, but it was really hard in those days. Students have it easy now. We didn't have proper embedding materials; we didn't have stains; you were just lucky if you got a good section. That was why I wanted to move to New York, because it was just such an exciting frontier, everything you looked at had never been looked at before. It was just like being the first one to go to the Antarctic, it was a period of just immense excitement.

I did the first electron microscopic analysis of what the cells were doing during regeneration. After we moved to Harvard I did begin to collaborate with John Paul Revel. We developed an autoradiographic technique with the electron microscope using the generating limbs as a model. Then I continued to collaborate with Revel when I began to work on the development of the cornea, which is one of my major interests.

Interviewer: Dr. Hay, could you describe for me your current research interests?

Dr. Hay: Well, I'm interested in tissue interaction in the embryo. I got into it because of my electron microscopic studies, which as I indicated, were on the regenerating limb in the beginning. These studies led me to work on the cornea. The ultrastructural information suggested that the epidermis was playing a very important role in the regeneration of the limb by producing extra-cellular matrix. So I moved into studying the role of the epithelium in development using a cornea as a system in the mid 1960's.

Since then I've been very interested in how extra-cellular matrix produced by the epithelium influences the further differentiation of that epithelium and also influences the differentiation of the fibroblasts that migrate into the sub-epithelial stroma at a later stage of development. In the lab at the present we're trying to dissect out that phenomenon at a cell and molecular level. We're interested in the possibility that all cells have receptors for extracellular matrix and their reaction to extra-cellular matrix varies during development. The real contribution of the work is to call attention to the fact that not only cells but also the matrix that they produce around them during development contains information that leads to the normal embryogenesis. So from the point of view of disease, the difference that this will make in your outlook is that you would not only ask — is there something wrong with the nucleus or the cytoplasm, you would also ask, has the extra cellular matrix been produced properly? At the moment we don't have a list of diseases in which we can point to abnormalities of the matrix as the cause. But I think in the future we will.

Interviewer: How do you actually carry out your research? Do you have a group of graduate students or colleagues with whom you work closely?

Dr. Hay: I have a small group, at the moment, two postdoctoral fellows. Steve Sugrue is working on the epithelium. In his research he has shown that soluble extracellular matrix molecules can affect the basal surface of the epithelium, can cause the cytoskeleton to take on a completely different configuration than it has in the absence of matrix. A second postdoctoral fellow, Jim Tomesac is analyzing the effect of the extra cellular matrix that the epithelium cells secrete on the migrating corneal fibroblasts which invade it. So he is doing studies of isolated corneal fibroblasts and also, at the moment, the cytoskeleton and the effect of extracellular matrix in the cytoskeleton.

My graduate student, Gary Greenberg, is interested in epithelial mesechimal transformations in the embryo and the effect of extracellular matrix on the shape of the cells and in the manner in which they migrate to their environment; and I have two technicians, so it is a small group.

One of the problems as administration increases is staying on the bench. I think it is extremely important for scientists to be on the bench. I do a major part of the electron microscopy on all of the projects that I mentioned to you. Obviously, I love electron microscopy and visualizing what cells are doing. I do most of my own printing of electron micrographs for seminars, lectures and that sort of thing. I make my own slides. I work in the culture room more or less. When I have a new group of people coming in, then I'm at the culture bench setting up the cultures. We have a moderate turnover, the technicians stay about two years if we're lucky and, of course, the postdocs stay about 2-3 years. So that means that there is a constant demand for me to be in the lab. Once a technique for setting up the cultures gets going, it's hard for me to find a seat in the culture room because the technicians and the postdocs are busy setting up the cultures. But, whenever we change a procedure or look for something new, I am there at the bench.

Interviewer: You spent a number of years, also, editing a journal?

Dr. Hay: Yes, the **Journal of Developmental Biology**. I took that on because I was mad at the way they were reproducing electron micrographs. It was a little peanut size journal up until about 1971. So I converted it into a very large-size page and introduced a number of reproductive techniques that they hadn't been using. The only way you could change their attitudes towards publication of electron micrographs, it doesn't do any good to write the editor, you have to be the editor, so that was why I did that.

Interviewer: Dr. Hay, you've recently edited a book on your area of interest. Could you tell me a little about it?

Dr. Hay: Yes. I took on the job because I really feel that extracellular matrix is coming into the forefront and finally cell biologists are realizing that not everything happens within the cell but rather that important things are happening out in the extracellular matrix. In fact, some of our research and the research of others indicates that extracellular matrix is actually telling the cells what to do. I was therefore attracted by the idea of editing a book on cell biology of extracellular matrix when Plenum Press approached me a couple of years ago.

Interviewer: Well, let's go into the issue of you as an Administrative Department Chair. How you divide your time, how you set priorities? You now have to juggle research, teaching, administration and anything else that may come up in terms of being a Department Head. Where do you spend most of your time?

Dr. Hay: Well, I haven't kept track, but I suspect that I spend most of it being Department Chairman, maybe half? I spend perhaps 30% of the time in the lab. It's very hard to say. I certainly spend more time being Department Chairman than any of the other activities that I like to do. I've cut down my teaching, I no longer teach Histology. And I really loved teaching Histology, being in the lab and running lab sections, but it's very time consuming to run a lab section, so I only teach Embryology and Developmental Biology. I teach an intense course in January to the medical students, which is a lecture every day for the month of January. So, except for the developmental biology course I give to graduate students with Joan Ruderman every other year, my teaching load is now relatively light. I had to do that because I had to have time to do my research. Obviously, from what I've told you about my career, the research is the most important part of my life.

Interviewer: Do you see any differences in the young women now studying medicine and your peers?

Dr. Hay: Yes. I think in the last five or ten years the whole attitude toward women has completely changed so that the women coming to medical school today, I think, feel very welcome. For one thing, she's no longer in the minority, she can expect at least 30% of the class to be composed of women. The attitude of fellow students toward each other is certainly different. Although, I don't think Mel Avery and I felt discriminated against, we clearly were kind of in a separate category from the rest of the class. We'll never know what we didn't get to do that the guys were doing.

Interviewer: As Department Chair, you're put in the position of counseling young people. How do you find yourself in that position right now when things for research look so dismal?

Dr. Hay: Well, I really can't believe that the picture can remain this dismal for a significant period of time. We have had downs and ups of this kind over the past 15-20 years and we've bounced back. We haven't bounced back with the kind of research money that we had in the 40's and 50's but we've kept going, and I really would tell any young person today that it's worth getting in there and fighting, I continue to be actively interested in research because I'm sure things are going to get better. Now we may have to wine and dine our congressmen and really pursuade the important people that research is as important as we think it is. I think the fact is undeniable, when you look at what has happened to basic science in the past 15 or 20 years. I couldn't have possibly predicted in my wildest dreams what we would know today. It's been a revolution and it's been because research has been funded by the United States Government. That's not a difficult story to sell a congressman. I really don't think that we'll be out of business. I think research has so much left to discover that we're going to make it. So I encourage young people to go into research.

autoradiography. The making of a graphic record obtained by placing a radioactive material in contact with or in close proximity to a photographic emulsion and developing the exposed film or plate.

basal surface. The bottom or primary layer.

cell receptors. In Ehrlich's theory of immunity, surface molecules of the cell which combine with foreign substances, such as toxins, antibodies, antigens, etc.

cornea. The transparent membrane, forming the anterior sixth of the outer coat of the eyeball.

cytoskeleton. The tonofibrils, keratin, or other filaments serving to act as supportive cytoplasmic elements, especially of certain epithelial cells.

differentiation. Specialization or the acquiring or the possession of character or function different from that of the original type.

electron microscopy. Investigation of minute objects by means of a visual and photographic microscope in which electron beams with wavelengths thousands of times shorter than visible light are utilized in place of light, thereby allowing much greater magnification.

embryogenesis. That phase of prenatal development involved in the establishing of the characteristic configuration of the embryonic body.

embryology. The science of the origin and development of the organism from the fertilization of the ovum to the beginning of extrauterine or extraovular life; in humans, the 2nd to 8th week of life, inclusive.

endoplasmic reticulum. The network of tubules or flattened sacs with or without ribosomes on the surface of their membranes.

epidermis. The outer portion of the skin.

fibroblasts. An elongated cell with cytoplasmic processes present in connective tissue, capable of forming collagen fibers.

histology. The science that deals with the minute structure of cells, tissues, and organs in relation to their function.

sub-epithelial stroma. The framework, usually of connective tissue, beneath the epithelium.

transformations. Metamorphoses; changes of form and shape.

Dr. Elizabeth Hay
General Questions

1. In what ways is Dr. Hay's research a team effort? What procedures does she especially enjoy and largely continue to do herself?

2. What difference does Dr. Hay see in young women now studying medicine and her peers?

3. What does Dr. Hay see as the future for medical research? What advice does she give to those entering the field?

4. What traits of the scientific researcher does Dr. Hay reveal? Why are these traits so important?

5. Given a limited amount of time, what are the potential conflicts that are confronting Dr. Hay as she attempts to deal with her administrative and investigative responsibilities?

6. Dr. Hay is involved with editing the **Journal of Developmental Biology**. Why did she feel compelled to take on this new activity?

7. Dr. Hay was also involved with editing a book on cell biology of the extracellular matrix. What were her reasons for taking on this endeavor?

8. What does Dr. Hay consider to be the most important part of her life?

9. Which would you find more rewarding, a career in research or in clinical work? Why?

Dr. Elizabeth Hay
Science Questions

1. Why was Dr. Hay so excited about electron microscopy in the early stages of her career?

2. What are the current research interests of Dr. Hay? Why did she become involved in this area of specialization?

3. Dr. Hay discusses the significance of the extracellular matrix in normal embryogenesis. What is the relationship between the extracellular matrix and normal embryonic development?

4. The field of biomedical engineering is producing many of the tools used in the diagnosis and treatment of disease, as well as an accumulation of basic knowledge of biological systems. The electron microscope is one of the tools. What are the advantages of this piece of instrumentation? What are the disadvantages?

5. There is a current theory that all cells have receptors for extracellular matrix and their reaction to extracellular matrix varies during development. What is the significance of this newly discovered interrelationship? How is this idea, about factors that influence embryonic development, different from the traditional ideas about control of development?

6. What is another example of molecules secreted by one cell interacting with receptors on other cells and influencing the behavior of these target cells?

7. Why will answers to the basic questions about fetal development be of benefit to people?

8. Suppose a particular molecule was identified as being the primary cause of abnormal tissue development/orientation in the fetus. The molecule in question influences how a group of cells align themselves. This incorrect alignment leads to a specific birth defect. How would this new information, possibly, lead to a treatment of the problem? What might the treatment involve?

Dr. Elizabeth Hay
Social Studies Questions

1. The development of a research team is part of the initial process in pursuing answers to a medical problem. How would you go about forming a team? What personality traits would you look for? What are the positive features of a research team approach to a medical problem?

2. What is it like to be a pioneer in a field as Dr. Hay has been in electron microscopy? Why might being a "pioneer" be especially helpful for women in medicine?

3. Where does much of the funding for basic research come from? What would be the ideal source of financial support? Do you feel this source of funding today is adequate?

4. In the funding for basic research, what is revealed about national priorities? Public awareness? How can individuals influence such policies?

5. Why is the ability to organize time and effort so important to success in research?

6. What ethical issues are raised by Dr. Hay's research, particularly as it applies to fetal development?

Profile #3
JANET McARTHUR, M.D.
Professor of Obstetrics and Gynecology

BIOGRAPHY

Dr. McArthur, who is well-known for encouraging women to enter the fields of medicine and athletics, began her career in 1943 as one of the first female residents admitted to the Massachusetts General Hospital. Among the first American scientists to obtain public funding for research in reproductive physiology, Dr. McArthur is both a practicing physician and a research scientist. Her major interests at present are in defining the endocrinological bases for the menstrual patterns of female athletes.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Gynecologists

Nutritionists

Exercise Physiologists

Immunochemists

Human Volunteers

Medical Equipment and Procedures Demonstrated:

Dietary Control in a Research Study

Controlled Exercise in a Research Study

Radioimmunoassays of Enzymes and Hormones

Gamma Radiation Counter

Social Concepts Discussed:

World War II and Professional Acceptance of Women

The Effect of the Women's Movement on Aspirations and Expectations

Decisions and Factors Affecting Career Advancement

The Importance of Collaboration in Scientific Research

Title IX — Equal Access to Athletic Opportunity

Transcript

Dr. McArthur: Sex research was not considered suitable to command Federal monies. I was really not respectable and it was really not until the population research pressure and the willingness of President Kennedy and President Eisenhower to throw their prestige behind this sort of thing that the NIH began to give any money to support this field.

Interviewer: The Joint Committee on the Status of Women has created and produced this series on women in medicine with senior women professors at Harvard Medical School. Today we're talking with Dr. Janet McArthur, Professor of Obstetrics and Gynecology.

Interviewer: Would you describe your current research interests?

Dr. McArthur: Yes, I'm engaged in trying to explain the reproductive disturbances of women athletes. This came about through a sudden bevy of about seven girls, who ran in to see me three years ago over a space of about two months, who had amenorrhea, a cessation of their periods, which was worrying them. They had been to see doctors who had said "you're having early menopause" and various alarming things and they wanted a second opinion. So I worked them up very carefully and discovered that the only common denominator, after ruling out these dire diagnoses, was that they were all athletes — they were all running long distances; they were doing middle distance races — things like the Bonnie Bell Marathon, and so on. Some of them, part of this group, volunteered to be subjects for more intensive studies. We did LHRH tests on them and we discovered that they actually had a superfluity of the gonadotropins in the pituitary so that when you gave the stimulus of LHRH they released more than normal amounts of these substances. Therefore, it was not a question of these hormones not being synthesized in the pituitary, it was that the hypothalmus did not release the LHRH needed to give them the peripheral levels of hormone.

That was very interesting and there was all this information beginning to accumulate about the endogenous opioids being secreted by stress. I knew that people who are morphine addicts have amenorrhea as a side effect. Therefore, it seemed logical to take the drug neloxone which is an anti-opioid drug which we use in our emergency wards to revive addicts who are narcotized, and try giving this to these women athletes and see what it did to their gonadotropins. We put an in-dwelling needle in their arm and sampled their blood every ten or fifteen minutes. Normally, there should have been frequent pulsations of LH coming out of the pituitary. We know now that these hormones are not released in a slow drizzle, but in packets every hour or two. Our subjects simply had a total flattening out of their LHRH release of the LH because they just didn't have these surges that they should have had. They just had a little titanic oscillation at the base line instead of these undulatory oscillations. But when we gave the neloxone, the opioid antagonist, there was a sudden surge of these hormones from the pituitary and the pulsations began to appear in normal rhythmic amplitude — just like lightening. So that did imply then that there must be some kind of chronic inhibition of the LHRH by the opioids perhaps, at least it was a good working hypothesis in athletes. So that then inspired us to organize a group of people to study it. So we got an exercise physiologist, Dr. Gary Schriner, at Sargeant College at Boston University. There is a big nutritional element, of course, in amennorrhea in many athletes, or many people with anorexia nervosa for that matter, who combine dieting and exercise in order to get even thinner, so we also recruited Dr. Beverly Bullen, who is a Professor of Nutrition at Sargeant College. Then we got radioimmunoassayists who could measure the particular hormones of interest. Dr. Dan Carr at the Mass. General who was able to measure beta

andorphin and beta lypotropin in the blood. Dr. Steven Repert who could measure melatonin which is another anti-reproductive hormone in the blood. These are things that are kind of available on a research basis but not a routine clinical basis. Dr. Inese Beitins in our laboratory who runs our radioimmunoassays took charge of measuring FSH and LH, the gonadotropic hormones, and estriol and progesterone, the sex steroid hormones. Well, the subjects have all been college girls that we've gotten over at Sargeant College. What we have done since then is to get an NIH grant to study this, (our consortium that I was describing to you) and we were doing it up at Sargeant Camp. Sargeant Camp is the locus that we have chosen for this work. It is a Boston University facility. It appealed to us particularly its attractive location and because it had these dietary facilities, and that it would be possible for us to control the diet of our subjects as well as their exercise.

Dr. McArthur: What about the composition of this diet that we're giving?

Dr. Bullen: Well, it was planned, as a result of the pilot study where we found that people increased their calories largely from carbohydrates. So we started people off in this study with 50% of their total calories coming from carbohydrates, 35% were fat sources, and 15% were protein. And, of course, the carbohydrate is very important to any runner who needs to fill glycogen stores in the muscles before these long runs so that they'll have the endurance to complete the run more readily than they would otherwise.

Dr. McArthur: How does this compare with the normal American diet?

Dr. Bullen: Well, whatever you call normal . . . but with the typical type of diet figures that we get, they're usually about 45% carbohydrate, much higher in fat, and then maybe 10-15% protein. Of course, it's very important to keep as a baseline.

Interviewer: Dr. Schriner, could you explain your role in this project?

Dr. Schriner: My role was to decide on a protocol for the girls, decide on what intensity, what duration, what frequency that they would exercise so that we may find out what would in fact affect the menstrual cycle. As far as the activity sessions, they start off the first week in doing about 2 miles in each workout, so that's 4 miles a day, 5 days a week. By the fourth week, they're up to 4½ miles per workout, by the fifth week, they're doing 10 miles a day — either one 10 mile run, or two 5 mile runs. So from the fifth week to the eighth week they do 50 miles per week.

Interviewer: What did you feel about the knowledge that's coming out of this study what it's doing to women's menstrual cycles?

Gretchen Von Mering: Obviously, it's something that's happened forever and it's just now that the scientific community is trying to get a hold on what is actually going on here. What it comes down to at a metabolic rate. What's happening. There have been a lot of qualitative studies done where they've interviewed a lot of women and found out what they felt like, how they react at different times during their training, this type of thing. But nobody has really gotten really into the baseline — what's going on. I think that's what's happening.

Interviewer: We were talking to each other earlier about the social implications of this research, that women have been for so long deprived of the opportunity to exercise and engage in physical activity. Now they are doing that and you're telling us my God, it messes up the menstrual cycle.

Gretchen Von Mering: But it doesn't really mess it up. As Dr. McArthur aptly put this morning in a discussion that she came up to talk to the women about, is that it seems that perhaps we can hypothesize that increased activity is actually what the body was looking for. Way back when we were cavewomen, the activity we had was up at about the level we have now at camp.— running around all over the place and our bodies have adapted to that, knowing that in a survival situation, there are only certain times when you should allow yourself to get pregnant and the body did that and it seems that that's exactly what it's doing now. It seems that it may be more normal for us not to have our menses every month than it is to have it every month. We'll see as the data starts coming in. There's going to be a lot of follow-up study on this.

Interviewer: Could you tell me how this piece of your research has grown out of other research you've done?

Dr. McArthur: Well, we couldn't have done it if we had not developed in our laboratory the capability of measuring the gonadotropic hormones and measuring them well. First, measured by biological assay with these hypothosectomized rats that I was telling you about, and then later with radioimmunoassay which we run in our laboratory and then most recently in what's called **in vitro** biological assay, which is going back to the rats again. Instead of injecting the preparation you're testing into the whole living animal, you kill the animal, take out the testes, separate the Leydig cells of the testes which are the responding agents. Then you incubate in a solution, these cells with either the test substance or the standard hormone and then you use radioimmunoassay to quantitate the testostone that those cells have secreted into the medium. That is a super sensitive system that also is biologically meaningful because only those hormones or fragments of hormones that will actually stimulate hormone production, testosterone production, will register in the system. Whereas radioimmunoassay is dependent on the characteristics of an antibody which might be responding to the biologically relevant part of the molecule where it might be a biologically irrelevant part. So we have all those capabilities in our laboratory and have been interested in them for years. Therefore, we could easily move in and do these techniques on athletes or whoever we were interested in.

Interviewer: Dr. McArthur, we were talking earlier about the rigors of academic medicine. How have you managed to keep your eye focused on research when you've had to do teaching, administration, and also clinical practice?

Dr. McArthur: Well, by restricting very severely my practice to reproductive problems, referring other problems; by very strict budgeting of my time. Part of the year, one's a teacher, you'll almost have to drop everything else; another part of the year, you can do your research, write your grant request or write your papers. It is a constantly revolving situation to try to keep all these balls in the air. When Harvard began taking women, I served a term on the Admissions Committee. And I've served on other committees since; search committees and so on. I have fitted that in naturally, as a matter of high priority and my duty to the school.

The only thing about it is that I hope the younger generation of women will get more committee experience younger than I did. I think it's important to get seasoned on committees when you can blunder and still be forgiven. By the time you get to middle age, you're supposed to know what you're doing and are not allowed as great a margin of error in your tactical handling of committee work as you are when you're younger. I very late in life got an appointment to serve on an NIH study section. That was a very good experience. It would have been invaluable to me twenty years earlier.

Interviewer: Dr. McArthur, you are still one of few senior women professors here at the Medical School. How has this visibility affected your career climb?

Dr. McArthur: I don't think it's easy to assess that. I can see, looking over my career as a whole, how social conditions affected it profoundly. That is, that I would never have gotten into a Harvard teaching hospital had it not been for World War II. I think that had something to do with admitting medical students to Harvard Medical School. After the war was over, when, say all the members of the MGH staff who had been in our hospital overseas returned, of course that made a profound difference in the milieu, and there were long years of very, very slow promotion, where it really seemed as if one would never receive any further increase in rank or anything. But then the women's lib movement sort of came in in the later stages of my career and I think that probably, you know, had something to do with my being given a professorial appointment.

Interviewer: You must find yourself in some ways a mentor to young women. What do you tell young women residents who want to go into academic medicine?

Dr. McArthur: Well, I tell them that it's a hard road and that whether they are men or women in academic medicine, they will not receive the kind of financial compensation that they would if they went into clinical practice, that unless they really love the work and are excited and rewarded by the things they find out in their work, that they shouldn't go into it. Because that may be almost their only substantial reward. But I think you have to have tremendous perseverance to do research because teasing new secrets out of nature is a very arduous task.

Dr. Janet McArthur
Vocabulary

amenorrhea. Absence or abnormal cessation of the menses (menstruation).

anorexia nervosa. A personality disorder manifested by extreme aversion to food, resulting in life-threatening weight loss and usually occurring in young women.

assay. Analysis; test of purity; trial.

endogenous opioids. Synthetic narcotics that resemble opiates in action, but that are produced endogenously within the body or cell.

estradiol. The most potent naturally occurring estrogen in mammals. It is formed by the ovary, the placenta, the testis, and possibly the adrenal cortex. **Estriol** is the metabolic product which can be found in female urine.

FSH. Follicle-stimulating hormone, secreted by the pituitary, and stimulates the monthly release of the egg from the ovary.

glycogen. Animal dextran; a glucosan of high molecular weight, resembling amylopectin in structure, but even more highly branched; found in most of the tissues of the body; the principal carbohydrate reserve, it is readily converted into glucose.

gonadotropin. Hormones capable of promoting gonadal growth and function. In female: FSH and LH; In male: ICSH or LTH.

hypothalamus. A part of the brain, the hypothalamus is prominently involved in the functions of the automatic nervous system and, through its vascular link with the anterior lobe of the hypophysis, in endocrine mechanisms; it also appears to play a role in the nervous mechanisms underlying moods and motivational states.

Leydig cells. Interstitial cells of the testis, responsible for secretion of testosterone.

LH. Luteinizing hormone, secreted by the pituitary gland, and which stimulates development of the corpus luteum.

LHRH. Luteinizing hormone-releasing hormone, a substance of hypothalamic origin capable of accelerating pituitary secretion of luteinizing hormone (LH), a glycoprotein hormone stimulating the final ripening of the follicles and the secretion of progesterone by them, their rupture to release the egg, and the conversion of the ruptured follicle into the corpus luteum.

melatonin. Formed by the mammalian pineal gland. It appears to depress gonadal function in mammals and is known to cause contraction of amphibian melanophores.

menopause. Permanent cessation of the menses; termination of the menstrual cycle in later life.

pituitary. Relating to the pituitary gland or hypophysis, an unpaired, compound gland suspended from the base of the hypothalamus by a short, cordlike extension of the infundibulum, the pituitary stalk. With the exception of the adrenal medulla and the parathyroid gland, the function of all peripheral endocrine organs depends heavily upon the proper functioning of the pituitary gland.

progesterone. Corpus luteum hormone; luteohormone; a progestin; an antiestrogenic steroid believed to be the active principle of the corpus luteum, isolated from the corpus luteum and placenta or synthetically prepared. Used to correct abnormalities of the menstrual cycle.

radioimmunoassay. An immunological (immunochemical) procedure to test for specific hormones: radioisotope-labeled antigen is reacted with (1) specific antiserum and (2) an aliquant part of the same antiserum previously treated with test fluid.

sex steroids. Hormones affecting sexual function and reproduction.

glycogen. Animal dextran; a glucosan of high molecular weight, resembling amylopectin in structure, but even more highly branched; found in most of the tissues of the body; the principal carbohydrate reserve, it is readily converted into glucose.

testosterone. The male hormone, the most potent naturally occurring androgen. It is formed in greatest quantities in the interstitial cells of the testes, is possibly secreted also by the ovary and adrenal cortex.

Dr. Janet McArthur
General Questions

1. What personal traits needed for a successful career in research are shown by Dr. McArthur?

2. How does Dr. McArthur plan and organize time in order to accomplish many demanding tasks?

3. What advice does she give to young women entering a scientific career?

4. What rewards and challenges does Dr. McArthur identify in her career?

5. When did research into sex related questions become respectable and receive federal funding?

6. What has been the focus of Dr. McArthur's research?

7. What historical events effected the career path of Dr. McArthur?

Dr. Janet McArthur
Science Questions

1. What are the current research interests of Dr. McArthur? What caused her to take on this area of investigation?

2. In a group of women who came to Dr. McArthur with reproductive disturbances, what was the initial diagnosis? With re-evaluation of their individual cases, what did she discover as the common denominator? How did this lead to a specific research project?

3. Some of the women volunteered for more intensive clinical evaluations. One of these evaluations consisted of measuring the levels of LHRH. What were the results of these tests? What was the significance of these findings?

4. What are endogenous opioids? What clue was offered to the research team, when it was stated that morphine addicts have amenorrhea as a side effect?

5. Neloxone is an anti-opioid drug. What was the observed effect in the women that were given this drug? What are the implications of this information?

6. What was the working hypothesis concerning reasons for amenorrhea established after some of the initial data was in?

7. Dr. McArthur organized a research team to investigate this problem. Who were the specialists that were recruited? What were their responsibilities?

8. What new hypothesis evolved out of the interpretation of early data that concerned increased physical activity in women?

9. What were the key clinical tests that were developed before this study? Tests which were previously developed in this laboratory?

10. Propose a model that explains how physical stress influences the amount of endogenous opioids secreted and how this could bring about the symptom of amenorrhea in women athletes.

11. The team approach to research, the division of labor, is illustrated in this tape. What advantages are generated by pursuing a research problem in this manner? Is this the way in which you pictured the process of medical research?

12. The process of disease diagnosis is not an easy task. There can be many causes for the same set of symptoms. What feelings do you have about the initial diagnosis, by some doctors, that these women were having early menopause?

13. What does her research show about the effects of stress? About the evolution of women? What assumptions are challenged? What are some possible social implications of these research findings?

Dr. Janet McArthur
Social Studies Questions

1. What two historical events especially affected Dr. McArthur's career in medicine?

2. Show how Dr. McArthur's research illustrates a model for a scientific study in the biological or behavioral sciences.

3. Describe the socioeconomic environment that influences Dr. McArthur's movement through the ranks of academic medicine. How is this environment different from the environment that exists today? How are socioeconomic conditions more positive or negative in the 1980's for career advancement?

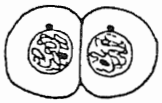
4. What stresses are there in a career like Dr. McArthur's? Are any of these stresses peculiar to women? Explain.

5. Why are social conditions so influential on career choice and development? How conscious are you of these influences on your future choices? Explain.

6. What is revealed about the evolution of women through Dr. McArthur's research?

7. What do women morphine addicts, anorexics, and runners have in common? How did Dr. McArthur use the discovery of this commonality in her research?

8. How does Dr. McArthur's research illustrate a model for the scientific study of behavior? For example, what old ideas are challenged? How is a working hypothesis set up? Why are a control group and a follow-up study used?



Profile #4
RUTH SAGER, Ph.D.
Professor of Cellular Genetics

BIOGRAPHY

As the discoverer of chloroplast DNA, Dr. Sager had a well-established career in plant genetics when her desire to explore the unknown led her to leave this research for human studies. She moved to England, became a student again, and learned techniques for genetic analysis at the cellular level. Now Chief of the Division of Cancer Genetics at the Sidney Farber Cancer Institute, Dr. Sager discusses the contributions of her research team to the growing understanding of tumor genetics. Dr. Sager compares the life of a scientist to that of an artist or dancer and says that "it gets to the very core of your existence."

VIDEOTAPE SUMMARY

Professionals Portrayed:

Genetists

Research Scientists — (Ph.D.s) — Colleagues, post-Doctoral Fellows

Ph.D. Students

Laboratory Technicians

Medical Equipment and Procedures demonstrated:

DNA Techniques — recombinant properties

Chromosome Studies — kariotype comparisons

Mendelian Ratios

Isoelectric Focusing

Social Concepts Discussed:

The Effect of The Women's Movement on Aspirations and Expectations

Decisions and Factors Affecting Career Advancement

The Challenge of a Mid-Life Career Change

Sharing Profession with Spouse

International Exchange of Scientific Information

Transcript

Interviewer: The most important contribution of your research, what would you consider that to be?

Dr. Sager: Well, I don't think I've made it yet.

Interviewer: The Joint Committee on the Status of Women has created and produced this series on women in medicine with senior women professors at Harvard Medical School. Today we're talking with Dr. Ruth Sager, Professor of Cellular Genetics.

Interviewer: Dr. Sager, could you describe your current research interests?

Dr. Sager: We have three areas. One is the DNA methylation area, the second is the rearrangement areas at the DNA level. The third area is a more genetic approach in which we have been transferring DNA from tumor cells into normal cells and from normal cells into tumor cells to look at changes in expression of knowing pieces of DNA which have been cloned out by recombinant DNA techniques. One technician, Constance Grabowy, has been doing very beautiful methylation studies at the DNA level.

Connie's research involves looking at the effects of a number of what are called "restriction enzymes," enzymes that cut DNA at particular sites in the DNA which they recognize by the sequence, the chemistry of that little location. Some of those enzymes will not cut, are not able to do this breaking of the DNA sequence, if there is a methyl group in the way, and we call them methylation sensitive enzymes. She has been going through all the restriction enzymes that are available, either from commercial source or from one's friends, to find as many methylation sensitive enzymes as possible in order to do a complete study of the positions of these methylated bases in DNA. She has been using chloroplast DNA as a model system for that. Although we're now beginning also to do this with human DNA.

A more fundamental area, I think, are permanent changes that result from rearrangement, and the jumping genes that I talked about earlier are an example of a mechanism for genomic rearrangement; another group in my laboratory have been working on this problem of genomic rearrangements. For example, Dr. Kiyoshi Tanaka has come from Japan and has been in my laboratory for two years. He is a physician and a researcher, both clinical and laboratory researcher in Japan, and in the last two years here he has found some very important clues of short sequences in DNA which seem to have an influence on this rearrangement possibility and the ability of cells to undergo rearrangement. He has found a region of mouse DNA which seems to be responsible for causing rearrangements to occur in a part of a chromosome which is adjacent to this region. He's been able to show that when this sequence is present, then the adjoining region undergoes continual rearrangement, and when it's absent, that region is completely quiet and does not undergo rearrangement at all.

Dr. Inder Ghadi is a talented cytogeneticist who is a postdoctoral fellow in my laboratory. He has been carefully comparing the chromosomes of normal cells and tumor cells to look for systematic changes in chromosome arrangements which may be occurring in the process by which a normal cell becomes a tumor cell. For this purpose, we've mainly been using Chinese hamster cells, but we're also doing some studies now with human cells, and there are a variety of methods. One of the methods is, if you have a recombinant DNA clone carrying a particular sequence of DNA, it can be used as a probe to find out whether that particular gene has undergone some rearrangement, has moved or has become amplified. Here, for example, is a cell in which there has been rearrangement many many fold, amplification of a gene that is involved in the resistance to the anti-cancer drug methotrexate. This is a study that has some direct clinical interest because methotrexate is one of the most popular drugs and very valuable drugs in the study of leukemia.

Interviewer: Can you explain how you made the jump from plant genetics?

Dr. Sager: When I got my Ph.D., I decided to leave corn genetics because by that time it became possible to do genetics with microorganisms, and everything moves so much faster that it was really sort of the threshold of the new era, and I wanted to be part of it. I decided to work on quite a different problem, but still it was a plant problem. I thought it was a plant problem. This had to do with indirect evidence that there were some genes that did not behave as if they were carried on chromosomes. They didn't show those nice three to one Mendelian ratio, and this became something that absorbed me for about the next 20 years of my life. Essentially, I discovered and established the genetics of what we call the second genetic system, which was the DNA located in the chloroplast.

One of the features of chloroplast DNA is that it has a very strange pattern of inheritance. Only the DNA from the female parent is transmitted to all of the progeny; the DNA from the male parent disappears and never reappears. We found that there was a molecular explanation for that, and it had to do with a special biochemical change in DNA, which is the addition of a methyl group; it is called methylation of DNA, which leads to exchange in the properties of the DNA, and when it is methylated it's protected from a particular enzyme. When it is not methylated, that enzyme comes in and just chops it up into little pieces. Methylation of DNA has turned out to be an important mechanism in mammalian cells where the control of gene expression is found. One of the really important things that we learn in the chloroplast work we've applied directly to the cancer problem. But after I had worked on chloroplasts for about 20 years there were lots of problems remaining. I decided to write a book about it and I wrote a book called **Cytoplasmic Genes and Organelles,** and it was hard work.

By the time I had finished the book, I was really tired of the problem, and I felt that I wanted to go on to something else. The problem seemed most challenging, and it still is one of the most challenging problems in biology: "how do normal cells become tumor cells?" That was a complete career change, you might say, because in 1972 I sort of became like a post-doctoral fellow again to start learning about clinical cancer to some extent and about cancer at the cellular level.

I spent a year in London in a wonderful laboratory, The Imperial Cancer Research Fund Laboratory. In Stoker's laboratory I really learned a great deal in the course of that year. Another person in that laboratory was Arthur Pardee, a very well known biochemist who had also switched from bacterial genetics to studying the cancer problem. By the end of that year we had decided to get married and that, I think, was a very important part of this new career of mine, because in the past I had always felt that I wanted to work on something that nobody else was working on and I loved the freedom of not worrying about the competition. But the cancer problem is more serious than that, and you really want all the help you can get, and the whole idea of talking to people who are interested in similar problems was new to me. I never talked to anybody about chloroplasts, just the people in my lab. So it was really very exciting to be married to a man who I could talk to about what I was working on even though our labs are completely independent and our approaches are very different. Still, I think it has been an enormous help to me to get another point of view because his point of view is very biochemical and mine is very genetic, so rather complementary.

Interviewer: Did you do collaborative research with him at anytime?

Dr. Sager: Never, never, no.

Interviewer: I want to talk a little about your climb through the academic ranks, professor. You were a professor at Hunter College. Was that something you actively sought?

Dr. Sager: Well, in a way it was. I was at Columbia University as a research associate supporting myself on my own grant; I guess it was called research scientist. But they would never give me an academic position. They just were not giving jobs to women. Everyone said, "You've written two books and you're internationally known, all that sort of thing, don't you think you ought to have a proper job?" But they were so very very hard to find and I still wanted to stay in New York, so I had a few reasonable job offers from elsewhere which I decided not to take. So the position that came up at Hunter College was really very attractive. The college had just become part of the City University, and they were building a graduate department; most of the people who had been in the biology department were old and retired, so that the department was being built from scratch. I was given a very good position; I only had to teach one course, which was rather unusual for City University, and they mainly wanted me to come and do research and attract more graduate students and faculty.

Interviewer: Do you have any pieces of advice for young women who want to pursue science?

Dr. Sager: I think the first thing is to be sure of your own abilities. Science is very demanding; you have to be able to think very well and also have a very good memory. You have to really love it; I think it all comes from inside; you feel that this is the way you want to live because doing science is a way of life. It really gets to the very core of your existence. It's not a profession like many other professions, its much more like being an artist or being a dancer. It's something that really demands everything from you that you are capable of. So you have to start with a fairer degree of assurance that that's what you like. But once you really feel that that is what you want to do, then you have to really stick with it.

Dr. Ruth Sager
Vocabulary

chloroplast. A plant cell inclusion body containing chlorophyl.

cytogeneticist. A specialist in a branch of genetics concerned with the structure and function of the cell.

DNA. Abbreviation for dioxyribonucleic acid.

DNA hybridization. Procedure used to identify DNA or RNA sequences by allowing separated known DNA strands to join with complementary areas on the unknown strands.

DNA methylation. Process to add a methyl group to any of the DNA bases; associated with regulation, expression and enzyme degradation procedures.

enzyme. A protein, secreted by cells, that acts as a catalyst.

Mendelian ratio. Mendel's law of dominance — where recessive traits only appear in individuals possessing only recessive genes, thus when two pairs of genes, one dominant pair and one recessive pair, are combined in a random manner, only one of the four possible gene combinations will yield an individual with the recessive trait.

methyl group. A group of the radical — CH3, present in a variety of compounds.

recombinant DNA. DNA produced by recombination or crossing-over between two homologous chromosomes.

restriction enzymes. enzymes which are able to recognize and break off specific sequences of the DNA chains; associated with identification: mapping techniques.

Dr. Ruth Sager
General Questions

1. What personal traits does Dr. Sager reveal that have aided her career as a scientist? For example, what does she, an internationally known scientist, mean when she says that she has not yet made her "most important contribution to research?

2. How is the team effort of research shown in Dr. Sager's work?

3. What direct clinical implications does the research in this lab have?

4. Dr. Sager says that she undertook "a complete career change." Why? How?

5. Describe the pattern which emerges in the development of Dr. Sager's career.

6. How does she illustrate the saying "publish or perish"? What influence did her publishing experiences have on her career?

7. What does Dr. Sager say about discrimination against women in academic medical research? How did she confront this discrimination?

8. What advice does she give to young women who want to pursue a science career? What does she mean when she says that "you really have to love it"?

9. How has the decision to marry influenced her career? To what extent does her husband's work relate to hers?

Dr. Ruth Sager
Science Questions

1. What area of research is Dr. Sager involved with?

2. What is recombinant DNA? Why are recombinant DNA techniques useful?

3. What is a restriction enzyme? What do they allow the research to do?

4. What is gene rearrangement?

5. Dr. Inder Ghadi, a cytogenticist, has been comparing the chromosomes of normal cells to tumor cells. He is looking for systemic changes in chromosome arrangements. What is the significance of these chromosome rearrangements?

6. Dr. Sager made a jump from plant genetics to cancer research. What were her reasons for making this shift?

7. Dr. Sager has made an important contribution to molecular biology. What was this discovery?

8. What does Dr. Sager consider to be one of the most challenging problems in biology today?

9. How might gene rearrangements on a particular chromosome be related to cell transformations? What might cause some of these gene rearrangements?

10. Dr. Sager is married to a biochemist. His lab is completely independent of hers. Do you feel that being married to a researcher in a similar field is an asset? Or is it detrimental?

11. What are the moral/ethical issues involved with recombinant DNA research? Should recombinant DNA research, because it has special risks, be allowed to be controlled in a self-policing manner, or, because of the magnitude of the safety issues, should this area of science fall under governmental regulation? What implications does this have for the researcher with a tradition of freedom of inquiry?

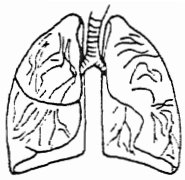
12. How responsible should scientists be for the consequences of the application of their research? In what areas of science and medicine are these concerns most evident?

Dr. Ruth Sager
Social Studies Questions

1. Whose responsibility is it to discern if discrimination exists in a profession or business? Whose responsibility is it to bring about change? Why? How?

2. What dilemmas arise in combining a career and marriage? Does medicine present special dilemmas? Explain.

3. Why might an established person choose to make a complete career change? Who might be affected by such a decision? How would a person make such a change?



Profile #5
LYNNE REID, M.D.
Professor of Pathology

BIOGRAPHY

Early in her career in England, Dr. Reid's discoveries in lung maturation and in respiratory diseases led to the development of a method for measuring lung hypertrophy known worldwide as the **Reid Index**. In 1974, Dr. Reid accepted an invitation to move her research team to Boston where she is now Pathologist-in-Chief of Children's Hospital. Dr. Reid explains how research breakthroughs in her laboratories lead to improved treatment of respiratory disease in children.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Pathologists

Research Scientists — (Ph.D.s) — post-Doctoral Fellows

Laboratory Technicians

Medical Equipment and Procedures Demonstrated:

Animal Models of Human Disease States

Catheterization of Blood Vessels

Light Microscopy

Carbohydrate Analysis by Chromatography

Radio-labelling and Electrophoretic Separation of Proteins

Electron Microscopy

Density Gradient Ultracentrifugation

Social Concepts Discussed:

The Significance of Mentors in Career Development

The Importance of Collaboration in Scientific Research

Use of Animals in Research

Decisions and Factors Affecting Career Advancement

Transcript

Dr. Reid: I'd been working with Mr. Haywood who was the thoracic surgeon and asked him one day what happened to the bronchi that didn't fill in bronchiectisis and he said perhaps you'd better find out, I don't think anybody knows and that, in fact, was the first thing that I studied.

Interviewer: The Joint Committee on the Status of Women in conjunction with the Office for Educational Programs has created and produced a series called "Women in Medicine" with senior women professors at Harvard Medical School. Today we are talking with Dr. Lynne Reid, S. Bert Wolbach Professor of Pathology at Harvard Medical School.

Interviewer: Under what circumstances did you come to Harvard?

Dr. Reid: I was invited to come and meet the committee that was appointing the new Wolbach professor and to consult. I hadn't realized they were inviting me to perhaps consider the chair, so I said that I wasn't particularly interested in moving from London. But they still asked me to come and consult, and one of life's ironies is that when I got here I realized that the facilities here were so good and the colleagues that I would be working with were such a splendid lot that I decided that I would accept the invitation. I was able to bring with me anyone that I wanted of my team, these people were mainly on soft money, so we weren't, as it were, taking away University departments. In the years before I came the inflation in English Universities had been running at a very high level, in fact 30%, so I was very fortunate because, in fact, the year I came, I would have needed to raise twice as much money to do the amount of work we'd done four years before. In fact, we have been very glad that we came to Harvard because we have been able to do a lot more here than we would have been able to do in England in the last five or six years.

Interviewer: And what was your previous position prior to coming to Harvard?

Dr. Reid: I had been Professor of Experimental Pathology and Dean of the Cardiothoracic Institute which is one of the Institutes of the British Post-Graduate Medical Federation, which is one of the medical schools of London University.

Interviewer: Dr. Reid, I would like to ask you to review what you would consider at this time to be the main contributions of your personal research and that of your department.

Dr. Reid: I would hope we have made contributions in several fields. Perhaps the one to tell you about first is the one that has developed particularly here at Harvard and that is really on the subject of pulmonary circulation. I'll also mention something about bronchial mucous, the diseases of mucous hyper-secretion and also about lung growth. Those have really been three things that have come through the work that I have been doing all my professional life. I suppose the thing that comes to mind first is pulmonary hypertension because we've just been given a grant from National Institutes of Health to start a special center of research here on pulmonary hypertension. We have been able to identify a variety of types of hypertension, some of them important in the newborn, some of them in the child, some of them the adult. So we've in the last couple of years really identified new diseases.

We have developed animal models for several types of pulmonary hypertension, in particular we have used the rat because of course it is small, it is cheap and we can do a lot more experiments with an animal that size. We have developed a way of leaving indwelling in the rat pulmonary artery, a catheter and an aortic catheter for up to two weeks. We were going to do a feasibility study for this at just about the time we left England and Dr. Nader suggested that we do them here in the cardiac research laboratories with Dr. Danville and Mr. Ronovitz. Mr. Ronovitz has since become very adept at putting in catheters. In our newborn work, we're studying the guinea pig, because we can in fact catheterize a newborn guinea pig. That has been very important because we've got therefore, the hemodynamic study so we know what the function of the circulation is and you can relate it to the structure, we can also use that model to look at ways of dilating the artery and ways of reducing, of reversing, the pulmonary hypertension. We've used the piglets and the sheep also. Dr. Brendi particularly developed what we call a high flow model that is a shunt for the pulmonary artery or from aortic to the pulmonary artery and reduce hypertension in that way. That mimics particularly some of the reasons for congenital heart lesions. The rat model we have been able to use to look at hypoxia, that is low oxygen as you might get at altitude or would commonly get when people are sick with pneumonia or all sorts of ways that their lung is disturbed. So that is hypoxia, and also oxygen toxicity, that damages and remodels the pulmonary circulation. So hypoxia, oxygen toxicity, high flow and also we have been able to use an alkaloid that will damage the endothelium of the circulation and cause pulmonary hypertension in that way.

One of the best things we do in either a human lung or an animal lung that we are studying is in fact to prepare an arteriogram which corresponds then to the sort of studies that are done in living patients, when we call them an angiogram. When we have prepared the arteriogram, we can still use the tissue for microscopic analysis so the sections are prepared in the ordinary way. You look at them down the microscope and we can use an image analyzer which is linked to the computer to make measurements, feed them into the computer immediately and then, of course, carry out the statistics that we want much faster than if we didn't have that sort of help. With those animal models, with the hemodynamic monitoring, with the structure taken from the light microscope through to EM and now through the cell level we hope we can establish what the basis is for some of the types of pulmonary hypertension. At the moment, some of the most new and important findings we have made, and that a number of infants who were born with pulmonary hypertension which we thought was simply because the lung hadn't responded, hadn't adapted properly at birth, but we now know that's not so. In fact, those lungs were abnormal before birth and at the moment our concern is to try to find out what it was that went wrong during pregnancy that in fact had interfered with the way the small blood vessels grew and developed and therefore influenced the way they are going to adapt at the time of birth. So that is one group. The group that is dealing with the infants, the newborns, the children with cystic fibrosis, they develop pulmonary hypertension because too little oxygen gets to their blood, so that's another very important problem we have here. Chronic bronchitis in emphysema patients, particularly the chronic bronchitis patients, they develop pulmonary hypertension, that's all part of the hypoxia story.

We are also interested in mucous hypersecretion. We all make mucous in our airways all the time as a protection. The normal person will produce secretion during a cold, but in a number of diseases, an excessive amount of secretion is important clinically, mainly to chronic bronchitis, cystic fibrosis, asthma. We've been able to apply techniques in the last five years that make it possible for us to recover all the large molecules that go into making the very complex slimy material that blocks up the airways. Dr. Basker, who is one of my colleagues here with us, he worked with Dr. Quint in London to develop or rather to apply to the study of bronchial mucous, a technique called density gradient ultracentrifugation. The importance of that technique is that we can take that very slimy stuff with such a mixture which is sputum, and of course, mucous from other parts of the body too, so the techniques that apply to mucous are going to be applicable to other studies, but he has developed this technique for taking total sputum, total bronchial secretion, treating it and we can recover virtually completely all the macromolecules that go to make up secretion. The importance of our findings at present are that we now know that it is not just the special secretion that makes the mucous or that we think of as the mucous or mucous glycoprotein that is important. There is a large amount of lipid protein glycans which seem important and hasn't been suspected before. So we are, I think, getting somewhere with analyzing the nature of the differences between diseases. We are able to take asthma, cystic fibrosis, chronic bronchitis, and by examining in this way, with this technique, the sol and the gel separately, we're finding that there are greater differences between the diseases than we have been able to identify by any other techniques.

Dr. Coles has been working with Dr. Basker and Dr. Stephen Coles has been using organ culture. This is something we developed in England with Dr. Jennifer Sturgis to find how in fact the bronchial glands are controlled and using human bronchial glands that we get from specimens that are removed at surgery, we have been able to look at the way the secretion from these cells is influenced and this is a way of sorting out what factors control them and so on. Now, of course, there are many new drugs and many new mediators becoming available that they are currently testing and Dr. Coles is able to work with Dr. Basker and to use these techniques to look at the secretion from the cells but by using radiographs we are able to identify which cells are secreting and how much of the sort. An important thing with all of this is then to quantify the behavior of the cell, individual cell types and to relate the activities we identify, either with electron microscopy or, autoradiography, to relate that to the sort of secretion they are connecting and analyzing.

Our third subject of particular importance at Children's is the way lung growth is interfered with by disease during childhood, and also by events that can go wrong before birth. One of the interesting things has been that we had worked with lung growth and we had done quite a bit at Brompton on diseases that affected the growing lung. This started I suppose originally because of my studies in bronchethisis and then in bronchitis. We found that there were a number of conditions that we would pick up in the adult that clearly had represented some interference with the way the lung of the child grows and these are what I would call again very clinical studies. We were studying surgical specimen and also autopsy specimen trying to sort out the way the lung had been disturbed by childhood disease.

Interviewer: Dr. Reid, many people know you for the Reid Index. Could you tell me about the development of that and its importance to your work.

Dr. Reid: I suppose it was one way of quantifying the changes that occur in chronic bronchitis. Most people, when I started my studies were mentioning that bronchitis was simply an infection, chronic infection. But it was clear that the basic change, whether infection was present or not, was the hypertrophy of the bronchial glands in the wall. The Reid Index represents a way of determining the degree of hypertrophy. It's easy, it's quick, it can be done just by a simple monocular in the microscope and I think it has stood the test of time.

Dr. Lynne Reid
Vocabulary

angiogram. Radiogram obtained in angiography, that is, the radiography of vessels after the injection of a radiopaque material.

arteriogram. X-ray picture of artery after injection of contrast medium into it.

asthma. A condition of the lungs in which there is widespread narrowing of airways, varying over short periods of time either spontaneously or as a result of treatment.

bronchiectasis. Dilation of a bronchus or of the bronchial tubes, usually caused by an infection.

bronchitis. Inflammation of the mucous membrane of the bronchial tubes.

catheter. A hollow cylinder of flexible material, designed to be passed through veins, arteries or even into various organs: heart, bladder, etc., to remove fluids for study.

cystic fibrosis. A congenital metabolic disorder, inherited as a recessive trait, in which secretions of exocrine glands are abnormal.

emphysema. Disease where the alveoli of the lung become distended or ruptured.

density gradient ultracentrifugation. Subjection to sedimentation, by means of the high speed centrifruge, of substances in a concentrated solution of cesium sucrose or other controlled substances.

gel. A jelly or the solid or semisolid phase of a colloidal solution.

glycans. Polysaccharides, carbohydrates containing a large number of saccharide groups.

glycoprotein. One of a group of protein-carbohydrate compounds (conjugated proteins), among which the most important are the mucins, mucoid, and amyloid.

hemodynamics. The study of the dynamics of the blood circulation.

hormone. A chemical substance, formed in one organ or part of the body and carried in the blood to another organ or part. Depending on the specificity of their efforts, hormones can alter the functional activity, and sometimes the structure, of just one organ or of various numbers of them.

hypersecretion. Excessive secretion.

hypoxia. Decrease below normal levels of oxygen in air, blood, or tissue short of anoxia.

macromolecule. A molecule of colloidal size, notably proteins, nucleic acids, and polysaccharides.

mucous. Relating to the clear viscid secretion of the mucous membranes, consisting of mucin, epithelial cells, leukocytes, and various inorganic salts suspended in water.

neonatal intensive care. The management and care of the critically ill newborn.

neonate. A newborn or neonatal infant.

oxygen toxicity. A body disturbance resulting from breathing high partial pressures of oxygen.

pediatrics. The branch of medical science that treats the children in their hygienic, physiologic, and pathologic relations; the specialty of the diseases of children.

preventive medicine. The branch of medical science that concentrates on the prevention of disease.

pulmonary hypertension. High arterial blood pressure in the pulmonary circuit. It may be primary, or secondary to pulmonary or cardiac disease.

sputum. Expectorated matter, especially mucous or mucopurulent matter expectorated in diseases of the air passages.

Dr. Lynne Reid
General Questions

1. Why did Dr. Reid come to Harvard?

2. How does her research illustrate the team work of scientific research? Give examples.

3. Why is a background in chemistry, physics, and math so essential for modern medical research? Give specific examples.

4. What dilemmas does a woman encounter in choosing a career in medicine? Explain.

5. What rewards are there in this work? What challenges? Would you consider a career in research or in medicine? Explain.

6. How important is it to have independence in one's work? What careers especially offer such independence? What are the advantages and disadvantages of assuming independence in a career?

7. What pattern emerges in Dr. Reid's career? How might you use this pattern in your own life?

Dr. Lynne Reid
Science Questions

1. What are the major areas of research that Dr. Reid is involved with?

2. What is a catheter? Why is it employed in hemodynamic studies of the lung?

3. How was the use of a computer integrated into the research process? What advantages were produced with this computer link?

4. What is mucous hypersecretion? With what clinical problems is it associated?

5. What is density gradient ultracentrifugation? How did this process aid the investigation of reasons for mucous hypersecretion?

6. What is pulmonary hypertension? How might it develop?

7. What new information was derived from density gradient ultracentrifugation studies of mucous generated from patients with bronchitis, cystic fibrosis, and asthma, respectively?

8. What is the Reid Index? What information does it give the doctor?

9. Investigate the phenomenon of pulmonary hypertension. What are the probable causes of this circulatory problem? What are the symptoms of this disorder in the newborn, the developing child, the adult? What are the problems associated with this disorder?

10. Biomedical instrumentation, in general, has greatly improved in the last decade. So has the computer. What advantages have been conferred on the researcher by linking the computer to medical research?

11. The use of various animals, in controlled studies, was illustrated by Dr. Reid several times. What are the experimental and statistical problems associated with using animal models in applied research?

Dr. Lynne Reid
Social Studies Questions

1. How did Dr. Reid discover her major field of research?

2. Describe Dr. Reid's career before she came to Harvard.

3. Why did she come to Harvard?

4. What contributions has Dr. Reid made through her research and that of her department?

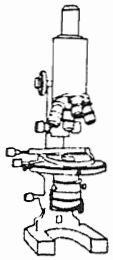
5. How are animal models used? Why?

6. What applications has this basic research had for humans?

7. How does Dr. Reid's work illustrate the teamwork found in research?

8. As revealed in the interview, what roles does money play in research? How has this financial factor influenced Dr. Reid's career?

9. What personal traits of Dr. Reid contribute to her professional success?



Profile #6
ALICE HUANG, Ph.D.
Professor of Microbiology and Molecular Genetics

BIOGRAPHY

As Director of the Laboratories of Infectious Diseases at Boston's Children's Hospital, Dr. Huang leads a team of physicians and scientists who are exploring virus structure and function. Dr. Huang explains how recent advances in peptide synthesis may lead to the development of vaccines for some of the world's worst diseases. Married to Nobel Laureate David Baltimore and mother of a young daughter, Dr. Huang talks of the decisions and problems involved in combining family responsibilities with a demanding career.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Virologists

Specialist in Peptide Synthesis

Research Scientists — (Ph.D.s) — post-Doctoral Fellows

Ph.D. Students

Laboratory Students

Medical Equipment and Procedures Demonstrated:

Homogenation and Sucrose Gradient Separation of Proteins

Iodination, Electrophoresis and Autoradiography of Proteins

Tissue and Cell Culture

Peptide Synthesis

Social Concepts Discussed:

The Significance of Mentors in Career Development

Decisions and Factors Affecting Career Advancement

The Importance of Collaboration in Scientific Research

Parenting, Day Care and Careers

Changes in Government Funding of Research

Transcript

Dr. Huang: He also said something which I will always remember, he said, "You know you have done very well here in the laboratory and you have a really good thesis." And he said, "Alice, the next few years will be very important and don't think that you are not going to have to work very hard, but I expect to see you a Professor some day." And it is that expectation, I think, which was important.

Interviewer: The Joint Committee on the Status of Women has created and produced this series on "Women in Medicine" with senior women Professors at Harvard Medical School. Today we're talking with Dr. Alice Huang, Professor of Microbiology and Molecular Genetics.

Interviewer: Was there someone at Hopkins that took you under his or her wing in terms of your science career?

Dr. Huang: Well, I have mentioned Barry Wood and he really started this special program and I was in my first year when the program started. There were 21 of us. He and his wife really did look after us very much in the first year, had us out to their home on Sundays, and he would play football with the boys and we'd all sit around and talk about science and medicine and people in science. I hadn't realized it at that time, but his wife was a microbiologist and had gotten a Ph.D. in microbiology while she had a baby in one arm and a toddler in the other hand. She was also the roommate to Polly Bunting and so the connections were very interesting. I think that they must have been extra supportive of women who were trying to make it in that world. After Barry Wood, when I ended up working in a laboratory and going for my Ph.D., my thesis advisor was Dr. Robert Wagner and I must say, I think that he was extraordinarily supportive. I was the first graduate student he ever had, and I think that all preceptors tend to put a lot into their very first student to make sure that things work out for them. He was good in not only showing me the important areas that one should do science in. He was also very good, I don't know if I should really say this but I will anyway, in saying that in science you are really judged purely on what you can do, not what your family was, what your father did, not on your social ability, but more on what you have in your head and how much you can produce. I think that was an important lesson to learn from him. He also said something which I will always remember. He said, "You know you have done very well here in the laboratory and you have a really good thesis," and he said, "Alice, the next few years will be very important and don't think that you are not going to have to work very hard, but I expect to see you a Professor some day." And it is that expectation, I think, which was important because as the next few years went on, I don't think I ever thought very much about where I was really going to end up. But in the back of my mind I remember that "I think you are going to be a Professor some day" and I thought, well, that's not a bad way to go and it sort of gave me a path to follow and aim for.

Interviewer: When did that unconscious career plan turn into something more conscious?

Dr. Huang: I remember that very clearly. It was at MIT. Annamarie Goriani Terrini was a research associate and I was at MIT as a research associate. She, of course, was much more established and well known and many students and post-docs came to MIT because they wanted to work with her. She said, "You may all be very happy doing what you are doing now as post-docs and research associates in labs where you are fairly happy," she said, "but think about it. Should your lab chief move away or die, which is just what happened to me, then you would be nowhere. Since you are in your late 20s and early 30s, it is time to really strike out on your own and build your own lab and establish your own reputation." She said, "Do it now because otherwise it is going to be too late." There I was happily being a research associate at my husband's lab, virtually had all the freedom I wanted, all the money I needed without worrying about it, but I listened to her and decided she was absolutely right. So then I decided that I really had to do it on my own, and I couldn't just stay and enjoy myself and do whatever I felt was easy to do. It was a luxury I think to live and work in an environment in which you had complete freedom but no responsibilities. So then I started job hunting. I interviewed both at Tufts, Boston University and at Harvard. So then I sort of waited around for Harvard and nothing happened at Harvard. Finally, I decided, whom do I know at Harvard? Well, the only person I knew by reputation was Dr. John Enders and so I made an appointment and I went to see Enders. It turned out, circumstances working out ways in which I really had no control, was that the department of microbiology and molecular genetics indeed had an opening for a virologist. But they didn't have space because they were renovating Building D-1. Ed Kass at Boston City Hospital was starting a group of virologists, and he needed someone who was really full time in the laboratory in order to help the fellows who were coming in as virologists. He had just finished off a top floor on the Channing Laboratory Building and needed someone to equip it and to organize it, so that the fellows who were interested in virology would have a place to work. So Enders knew all of this and I think, I am not sure of the exact story, but I think that he ended up putting Kass and the Department of Microbiology together and the Department was willing to give me an appointment and to have me do my teaching function in the Department. Ed Kass was willing to give me a physical location. And so like everyone else in my age group at that time, I put in for a grant for $50,000 for three years and I got it. Ed Kass said, "This is the first time someone here has ever done that; I guess you're fairly independent," and so I started rolling that way.

Interviewer: So getting an independent grant was a very important step for you?

Dr. Huang: Oh, I think it was and I think you know it is unfortunate these days that it is much harder for a young person to start. I mean, in the late 60s and early 70s, it was assumed that someone in my field would get a grant as an assistant Professor, get almost all their major equipment which would be between $30,000 to $60,000 and just start going and set up a lab de novo, out of nothing. And that was just what everybody did. Now I think that the institution has to come up at least with starter funds and some heavy equipment.

Interviewer: Could you describe some of the problems that people in your lab are working on?

Dr. Huang: I would be happy to. One of the problems that is being worked on is the continuation of the questions involving defective particle interference, defective interfering virus particles, and this is work being done by Dr. David Cave. The project that we thought would be best, would be to isolate DNA molecules that were copies of RNA sequences of the defective interfering virus particles that we know about, and taking that DNA ask, "If you can use it as a probe against the products that were made in living animals, such as mice. To look at the products that were made of brains or spleens or anywhere else and ask what the DNA would do, would they hybridize and light up sequences if they were identical?" So in this way we can ask the question, "Do defective interfering virus particles alter the course of a given disease?" Will it ameliorate the disease? Will it cause it to be more persistent rather than acute and to really prove it by showing how the genetic information is being replicated in these animals and in the particular time frame. So what he has had to do in the last year or so, is to be able to handle DNA in plasmids, to grow them up in bacteria, to be able to translate them so that they will be labeled with P32 in vitro and then to develop the methods of hybridization in the laboratory that would be useful for his purposes. He has actually been very good in reading the literature and adapting new methods — the brain is not the easiest organ to work with. He has been highly successful now in getting nucleic acids of the right size so that we can actually prove whether defective interfering particles are there or not there. So I am very pleased with what he is doing. That is Dr. Cave.

Then I have had a post-doc named Dr. Lynn Little who has been with us for a year now. His background was really in viral pathogenosis and he has done mostly animal work. He started working on growing vesicular stomatitis virus in human tumor cells. We have had the collaboration of Dr. Judah Folkman, who has supplied us with primary cultures of human tumors that he has actually gone in and taken out of patients. This particular work is getting to the point at which we think we have our hands on the tumor specific human antigen which is found on HeLa cells but is related to neuroblastoma and rhadomyosarcomas in children, so we are fairly excited about that.

I have been very lucky in our lab to have had a chief technician named Trudy Lanman who has been with me since 1975. One of the most professional technicians that I have ever seen and not many laboratories really of my size, have only one technician. She is the one who does all of the ordering, all of the maintenance of the laboratory and besides she keeps up the tissue culture and the virus assays in the laboratory.

We have a new venture that is going on in the laboratory now and it is sort of fun! In fact, it comes in the appearance of a big machine and it is called the peptide synthesizer. It is an automated computerized system that really does simple organic chemistry reactions. The reason that we have it is because there has been a new, let's say, a new discovery of an old discovery, that has happened in the past two years and this has really accelerated by discoveries made out in San Diego. Now what they found was that you can make a peptide of several amino acids hooked up. It doesn't have to be very big. It could be anywhere from six amino acids long, up to 20, and these amino acids are actively hooked together, can be then injected into rabbits and elicit antibodies. That antibody will be able to find the big protein molecule of which the peptide is just a part of. So what that says, is that just for molecular biology, you can now begin to map out specific domains of that protein. You can also use the antibody to purify the protein out of a gamisch of other things.

Also, there is tremendous potential for this peptide as a vaccine because instead of having to take a whole organism, whether it is a virus or a bacteria and try to kill it in some way, or to

attenuate it and inject it into people as a vaccine to protect them against the more virulent kind, we now can just synthesize the peptide of the region that we are particularly interested in. That, we know, will elicit protective antibodies in the human host and just use that clean preparation, inoculate it into people and protect them. In fact, over the last few years, the last two years, there have been reports for both hepatitis B virus and for foot and mouth disease virus that such peptide vaccines work very well. These results now are in animals, but I see no reason that they won't be extended to humans very shortly, so for an infectious disease division it makes good sense to get into this particular area.

Now I have have been very lucky in the person I found, the people who know organic chemistry and know solid phase peptide synthesis are actually very few in this country and I was lucky to find Dr. Janice Young who had been doing this ever since her days at Berkeley when she was a post-doc. She, in fact, has coauthored a book called **Solid Phase Peptide Synthesis** with John Stuart, so she comes highly equipped to run the facility, to trouble-shoot and to really take care of it.

Interviewer: I would like to talk a little about your family life, your life outside of the medical school here. You are married and you have a child. Was that a difficult decision, to have a child?

Dr. Huang: Oh not at all. I think that, well my reasoning went this way: That you only live once and there are so many experiences in life that one should try to have as many as possible.

Interviewer: How has that affected your career development?

Dr. Huang: That is a very interesting question. I think that before I had a child I would always look at women and say, these women who just quit after having their first child and said, "I am dropping out and I am going to raise a family," that they were just using it as an excuse and that they really did not enjoy what they were doing to begin with. When I had my first child, I realized that that was a rather snap judgement. The hormones do an amazing job on one's head and you are just not in control of what you feel and what you think. I was lucky enough not to have had my child until I was about 35, so my career was fairly well established. I had a functional laboratory with several people who were actively involved and so it wasn't necessary for me to be at my 100% best. So even though I think at times I found it very difficult to concentrate, and to be perfectly honest, I don't think I really got my head back under my own control for two years after the birth of my daughter.

Interviewer: Would you advise women in science to delay child bearing until their career is well established?

Dr. Huang: I think that would certainly help. I think that there are two, well there are several things. One is that financially one should be in a position where one has enough money to know that you can hire the best care or put your children in the best day care centers and not try to pick up babysitters here and there and try to make do. I think having that stability just makes life a lot easier and then you never have to worry about what is happening to your baby when you are at work.

Interviewer: Do you encourage young women to pursue science and to stick with it?

Dr. Huang: I encourage young women to find themselves and to use whatever potential they have to the fullest. Since I know science best, I tend to use that as a jumping off point. I can at least show them how exciting an area it is, how much fun I have had doing what I am doing, and I think that is one area that I do push.

antibody. In any broad sense any molecule, soluble or cellular, which is evoked by the stimulus provided by the introduction of antigen and which reacts specifically with that antigen in some demonstrable way; specifically, one or other of the classes of globulins present in the blood serum or body fluids of an animal as a result of antigenic stimulus or "naturally."

attenuate. To reduce, by heat or chemical action, the virulence of a pathogenic microorganism, prior to use as a vaccine.

defective interfering virus particles. Imperfect or malfunctioning virus particles which otherwise would produce superinfection, mutual extinction or cell blockade when exposed to another virus in a susceptible cell, in some instances at the same time and in other instances at different times.

DNA. Abbreviation for deoxyribonucleic acid: the large protein containing deoxyribose as the sugar component and four bases: adanine, quanine, thymine and cystosine. These are arranged as two long chains which are twisted into a double helix. DNA is found principally in the nuclei of animal and vegetable cells, usually loosely bound to protein is considered to be the autoreproducing component of chromosomes and of many viruses, and the repository of hereditary characteristics.

DNA hybridization. Procedure used to identify DNA or RNA sequences by allowing separated known DNA strands to join with complementary areas on the unknown strands.

Foot and mouth disease virus. A picornavirus (very small ether-resistant virus having RNA nucleic acid composition) causing foot and mouth disease of cattle, swine, sheep, goats, and wild ruminants.

HeLa cells. The first continuously cultured human malignant cells, derived from a carcinoma of the cervix; used in the cultivation of viruses.

hepatitis B virus. Serum hepatitis virus; the causative agent of viral hepatitis type B, a virus disease of the liver.

in vitro. In the test tube, referring to chemical reactions, fermentation, etc. occurring therein.

microbiology. The science dealing with microbes (microscopic and ultramicroscopic organisms).

molecular genetics. The branch of science that deals with heredity at the level of the molecule.

peptide. A compound of two or more amino acids in which the carboxyl group of one is united with the amino group of the other, with the elimination of a molecule of water, thus forming a peptide bond, --CO--NH--.

peptide synthesizer. An automated system that produces specific small peptide bonds, by joining the carboxyl group of one amino acid with the amino group of another amino acid, with the elimination of a molecule of water.

plasmids. A paragene or replicating unit, other than a nucleus gene, that contains nucleoprotein and is involved in various aspects of metabolism in organisms; extra-chromosomal hereditary determinants.

rhabdomyorsarcoma. A tumor, usually highly malignant, of striated muscle.

neuroblastoma. A malignant neoplasm or tumor characterized by immature, only slightly differentiated nerve cells of embryonic type.

pathogenesis. The mode of origin or development of any disease or morbid process.

RNA. Abbreviation for ribonucleic acid, a macromolecule/protein consisting of ribonucleoside residues connected by phosphate from the 3′ hydroxyl of to the 5′ hydroxyl of the next nucleoside, involved in the basic processes of protein synthesis.

tumor specific human antigen. Any of various sorts of material (e.g., microorganisms, toxoids, exotoxins, foreign proteins, foreign cells or tissues and others), specific to various tumors in humans, that, as a result of coming in contact with the appropriate tissues, after a latent period, usually of from 8 to 14 days, induces a state of sensitivity and/or resistance.

vaccine. Any preparation intended for active immunological prophylaxis — preparation of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; microbial, fungal, plant, protozoal, or metazoal derivatives or products.

vesicular stomatitis virus. Apparently an RNA virus, agent causing vesicular stomatitis in horses, cattle, sheep and pigs, with lesions similar to those of foot and mouth disease but milder clinical reaction.

virology. The study of viruses and of virus diseases; **virologist**, a student of virology.

virulent. Extremely dangerous; denoting a markedly pathogenic microorganism.

virus. A term for a group of **microbes** which with few exceptions are capable of passing through fine filters that retain bacteria and are incapable of growth or reproduction apart from living cells.

Dr. Alice Huang
General Questions

1. Define the term "mentor." Who were the mentors in Dr. Huang's career?

2. How did mentors set the expectations, point the way — or, as Dr. Huang says, give her "a path to follow and to aim for"?

3. What specific female role models did she have? Why were they especially helpful?

4. What personal traits helped her to advance in a research career and to make important personal decisions about marriage and family?

5. Dr. Huang made an important career decision while she was still young. What was this decision? Why was this early decision such an important one in terms of developing a career in academic medicine?

6. Dr. Huang had a misconception about women who leave their careers after having their first child. What was this misconception? Why did she reconsider her perception of women's commitment to their careers?

7. According to Dr. Huang for what reasons should women in science consider child-bearing?

8. What steps to success are revealed in the career pattern developed by Dr. Huang? How did she position herself for advancement? How did she use networking?

9. Why does she describe her work as "fun"? Why is that significant?

10. Using the information Dr. Huang gives about her career development, write a set of guidelines on how to advance.

11. How important is it to enjoy one's career work or even to find it fun? List the characteristics of your ideal career income, status, etc. Where would you rank enjoyment of work? Why?

Dr. Alice Huang
Science Questions

1. What are viruses? How do they cause disease? How are they transmitted?

2. Why is there difficulty in showing a cause and effect relationship between specific viruses and certain diseases, such as cancer?

3. What does her work show about the team effort of research?

4. How does Dr. Huang illustrate the personal traits suitable for leading a medical research term? What are these traits?

5. The peptide synthesizer is an automated system designed for the production of very specific small peptides. Vaccines for particular viral infections could be developed using this piece of instrumentation. Elaborate upon this procedure.

6. Using DNA hybridization techniques, how might one determine the presence of a viral genome in a transformed cell? How could autoradiographic labeling with P^{32} aid this problem?

7. What are the current research problems being dealt with by Dr. Huang's lab team? Why will information acquired in this area provide immediate and long term benefits?

8. Medical research needs financing. Where does the money come from that supports current medical research? What are the current problems with financing medical research?

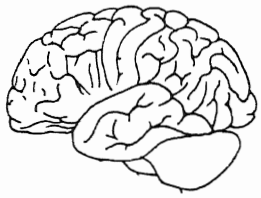
9. What is the significance of showing the presence of defective interfering particles in transformed cells? How might this be accomplished?

Dr. Alice Huang
Social Studies Questions

1. Why are role models so important to success? When role models are limited, how can a person set about building new opportunities? How can school, education, or families help people who are trying to break out of stereotypes as seen, for example, in "Women In Medicine"?

2. What conflicts can arise when combining a medical career and family? How might these conflicts be resolved?

Profile #7
MARGARET BRENMAN-GIBSON, Ph.D.
Professor of Psychology



BIOGRAPHY

Dr. Brenman-Gibson, one of the first to use hypnosis in the treatment of psychological problems, especially war neuroses, discusses her early studies at the Menninger Clinic, and how World War II provided research opportunities for herself and other women. Her recent research has focused on patterns of creativity and a psycho-analytic biography of the playwright Clifford Odets. She explains how she combines work with marriage to playwright William Gibson and with motherhood. She is an outspoken and active worker in the anti-nuclear movement.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Psychologists

Psychiatrists

Playwrights

Medical Concepts Discussed:

Use of Hypnosis in Treatment of War Neuroses

Creativity Compared to Hypnosis

Social Concepts Discussed:

World War II and Professional Acceptance of Women

The Effect of the Women's Movement on Aspirations and Expectations

The Importance of Collaboration in Scientific Research

Role Reversal in Marriage

Parenting

Anti-Nuclear Movement

Transcript

Interviewer: The Joint Committee on the Status of Women has created and produced a series called "Women in Medicine" with senior women professors at Harvard Medical School. Today we're talking with Dr. Margaret Brenman-Gibson, Professor of Psychology at Harvard Medical School.

Interviewer: The main area of interest which you have studied has been in the area of creativity and hypnosis. Were you considered somewhat of a maverick among your colleagues for choosing to make this an area of research?

Dr. Brenman-Gibson: Oh sure. I was considered a maverick for marrying this improvident artist in the first place. Yes, definitely, by my family as well. But I would say that yes, the choice of, first of all, hypnosis, which involves an altered state of consciousness which is, in my opinion, not qualitatively different from that state we call the creative state. This means a state in which you are, to some degree, letting go of what we might think of as the most conscious, rational, analytical, logical — all the things that have been called either masculine modes of thought or that have been called left brain thinking, all of that stuff. All of which is altered to some degree by the thing we call hypnosis is probably not that different from the state in which you are open enough to yourself to be creative. Indeed, in the book that I wrote with Merton Gil called **"Hypnosis and Related States,"** there is a chapter on hypnosis and the creative process, in which precisely what I was just alluding to is discussed in some detail. It seems to me I knew way back then — we're talking about 1959 or something like that which is like twenty-four years ago. I think I knew then, not as clearly as I do now, that it takes an altered state of consciousness for us to enable ourselves to be more open to ourselves than we normally are. Most of us, most of the time, are hanging on to some kind of analytical, logical, rational hold on outer reality in a way which is necessary for survival. I mean, that's why we have those functions but which also, to some extent, put brakes on that more clearly flowing thing which puts together things that normally you would think don't go together — that integrates things that have been polarized.

Interviewer: Fairly early in your career you had the good fortune to work with people who believed in your talents. Tell us about your relationship with, who then was your mentor, Robert Knight.

Dr. Brenman-Gibson: Well, that was actually in the first year I was at Menninger's, and I had learned from Wells at Syracuse University the incredible technique of hypnosis, which he had learned from Morton Prince and William James, if you can believe. This goes back quite a way. Now Robert Knight was then Chief of Staff at the Menninger Clinic in Topeka, Kansas; and when I gave a seminar, really at the invitation of Karl Menninger, at the end of which Karl Menninger had said — I'll never forget it, it made me so happy — as I was leaving the room, he shouted to Robert Knight, "Don't let that girl get away." Robert Knight, who knew I was stationed down at the Children's Division of the Menninger Clinic, which was the Southard School, named after our Southard here in Boston — Robert Knight then wrote me a note and said, "It's a pity for you to keep hiding your light under a bushel down in the

Interviewer: What are the rewards of working in an academic setting?

Dr. Brenman-Gibson: I would say the essential reward of working in an academic setting, provided that you are at the same time continuing your clinical work, is the breadth of the intellectual bases that are touched in an academic setting and that are made infinitely more accessible to you. I don't think it's possible, really even in the most sophisticated clinical installation, to begin to match the richness and the scope and the range of intellectual nutrition that a really good academic setting, particularly this one, offers. This is unique in the world, as far as I can see.

Interviewer: You're married to playwright William Gibson.

Dr. Brenman-Gibson: I am.

Interviewer: You were very involved in your career at an early age before he became a successful writer. How did this affect your relationship?

Dr. Brenman-Gibson: At the time it was all happening, early in my career when I was the breadwinner, and he was, really, the non-earning poet in the family, as far as I knew then, there was no real problem. But as we looked back over it, you know, later, it seemed to both of us that he had been harboring kinds of resentment, kinds of humiliation, at being regarded as my adjunct, my worser half, I suppose you'd have to say, "Mr. Brenman"!

Interviewer: Was there competition in your marriage?

Dr. Brenman-Gibson: Again, it's a question of how conscious it was when. I would say the competition in our marriage is infinitely more conscious now than it ever was in the early days because in the last year and a half, I have been very happy with the success of the book that I wrote called **"Clifford Odets: An American Playwright".**

Interviewer: What Clifford Odets?

Dr. Brenman-Gibson: Well, I think that's really answered — in a way I think I may even answer it in the book itself — which is that when I was growing up the 'thirties, the culture hero for all of us, including for my husband, was Clifford Odets. He was the playwright who really gave voice to what all of us were feeling then — the necessity historically at that time, which was to say, we must make a world where this creative human potential will have its best chance to flower and grow and enrich all of human life, not just the person who's making the art, but people who are enjoying it. And it's a whole view of life which . . . is essentially very humanist and has values which are exactly at the opposite ends, for instance, of the present values that I am running around the country opposing, namely, that we must destructively win over the other guy rather than creatively allow everyone in the world not only to eat but to live the most — to realize their own potential, you know? Clifford understood that.

Interviewer: You said you met your husband at the age of 17 or 18, and you have been married since, I imagine, your early 'twenties. During the early years of marriage, you and your husband made a conscious decision not to have children, because you were pursuing your training. When did that decision change and why?

Dr. Brenman-Gibson: Oh, I think that's probably pretty simple, and it has to do with the life cycle. It didn't become acute, I would say, until the next large figure was being approached, which was 35. Along about that time, I began to get really unsure, very conflicted, about this. I

Children's Division. Soon you will be brought up here to the really important main building, and you will be appointed a research fellow." This was after I had given my very first seminar on hypnosis which they were interested in at that time because this was already during the War, and what was being sought during the War was some way of dealing with the traumatic war neuroses in servicemen who were coming back in droves from the front. People who had been in some hideous kind of combat and who were then having nightmares or other kinds of bad disturbances, who could be helped with hypnosis, as it turned out. So that was a little bit later after the seminar, but I think probably the reason, aside from the fact that Karl Menninger was an intrepid explorer in this field — he was one of the first psychoanalysts in this country — and aside from his own acts of courage in this regard, I think the necessities of the time, which was the War, encouraged them to allow me to really do research in this field. Also to allow one of their talented residents in psychiatry, who was Merton Gil, to work with me, even though at that time, unlike now, hypnosis sounded to most people like something very peculiar and a little quirky and weird and, you know, kind of suspect. At the same time, and I must say that I admire to this day Karl Menninger's wild, intrepid capacity to look into anything that held promise — so it was that which started that whole thing. We got an NIH grant which went on for many years.

Interviewer: Were you the only woman in that setting?

Dr. Brenman-Gibson: Yes.

Interviewer: Was there a reluctance to take you under Knight's wing, or did Menninger at all hold back because you were a women?

Dr. Brenman-Gibson: That was not obvious to me at the time. I'm sure that that was there, but you know, I almost hesitate to say this because it's terrible: The fact is, I do believe that one of the reasons I moved as fast at the Menninger Clinic as I did was precisely because it was during the War years when many of the young, gifted men who would have been psychiatric residents or whatever — research people — at the Menninger Clinic, were in the War. Many of them. It's, in a way, a foolish thing to say because it was, after all, staffed by men (the Menninger Clinic) and there was nobody else, man or woman, besides me who was doing this kind of research in hypnosis, certainly not on a theoretical basis to explore creativity or to help the war neuroses. I'm not saying that I had no talent; I'm sure I had some talent at that point, but I think that my acceptance was made easier by the fact that so many of the gifted men were simply in the service. I think women have an infinitely more difficult task in life. I really do, you know.

Interviewer: Given the constraints of the professional market?

Dr. Brenman-Gibson: Absolutely. Given the constraints of what we have been "allowed to do" or not do over centuries and centuries. When I talk about maintaining one's feminine identity, I by no means am saying let us give up the hard won territory that we have gained. Oh, not at all. I think it's outrageous, for example, that at this really wonderful University, Harvard University, one of the finest in the world, maybe **the** finest in the world, that among the professors at the Harvard Medical School (actually 300), there are only ten of us who are women!

was still conflicted, I would say, as I guess I might have mentioned to you earlier, was conflicted enough that I asked Margaret Mead what she thought about this. Could women have a career and children at the same time? She said, "No problem." That's really when we started to plan having a family. I have two sons. I would not, for a moment, feel that I would have done better had I not married and not had children. Indeed, as I was telling you earlier, I feel that my own life is infinitely richer for reasons of having gotten married and having children. I don't say it has been easy; it has **not** been easy; it's been very difficult, particularly in the first ten years of their lives.

Interviewer: You are very involved right now in nuclear disarmament, lecturing, going around the country talking about this issue. Why did you choose to take this on?

Dr. Brenman-Gibson: After a great deal of soul-searching and really serious thoughts, it became very clear to me that unless those of us who really see the situation clearly, namely, as something that's going to end the planet unless we do something about it, I felt I had to make this one of my highest priorities. I feel this is really beyond anything one could call narrowly political, and I feel that it's essentially a question of education and that unless I, among others of course, help to really educate people to know that the situation, as it stands now, is on a course, that if we don't change that course, we're going to end up where we're heading, which is in a mutual, assured destruction between the U.S. and the Soviet Union.

Interviewer: You are a full professor at Harvard Medical School. Did you ever consider how your outspoken nature and political involvement would affect your reputation among your colleagues?

Dr. Brenman-Gibson: Yes. I have considered it very seriously, and I'm sure that in some quarters it has, as they say, not done me any good. On the other hand, when you consider that all of life involves weighing one set of risks against another, I feel that the risks involved in taking a chance on my reputation, on my standing, or my possible further advancement or whatever, that those risks become nothing, zero, unimportant, compared with the risks that are involved in ignoring the danger this planet is now in. It has become for me such a high priority that I must confess to you that two weeks ago, after really a very long period of soul-searching and deep thought about it and of very sleepless nights, I elected to do my very first civil disobedience action in New York City in front of the Sperry Corporation, which makes most of the component parts for the Euro-missiles, and 21 of us were arrested. I feel very proud of that, you know? I rather like the idea of a professor at the Harvard Medical School engaging in something that really says very clearly, "you are going to have to arrest American citizens of all kinds, not just young, rebellious people who don't like war and who are known to be idealists, but you're going to have to arrest **respectable people**."

Interviewer: Do you think you would have been as likely to have made the same decision had you been at a different point in your career, say a young, aspiring assistant professor?

Dr. Brenman-Gibson: That's a very good question, and I ask myself that as well, wondering, am I being so "courageous" precisely because I have come, I suppose, as far as you can come, you know, in terms of professional advancement? It's reasonably secure, I suppose. I don't imagine getting arrested for nonviolent civil disobedience with a religious interfaith task force would quite be regarded by an ethics committee as a 'bad' thing. How could they think that? Yet, I think about it, sure. I'm not sure I would have made the same decision if I'd been 32 or something like that. **I would like to think I would have.**

Dr. Margaret Brenman-Gibson
Vocabulary

consciousness: (1) the state of awareness; (2) the totality of experience at any given moment as opposed to mind which is the sum of past consciousnesses; (3) awareness of acts, activities, and reactions; (4) the subjective aspect of neurological activities; (5) self-knowledge, self-awareness (Chaplin).

creative. Pertaining to productive mental application or functioning — usually with the implication of employment of information derived not from direct experience or learning but from conceptual extension of such sources — in the solution or the development of artistic or mechanical forms (Chaplin).

creativity. The ability to produce new forms in art or mechanics or to solve problems by novel methods (Chaplin).

hypnosis. Hypnotic state; an artifically induced trance-like state resembling somnambulism in which the subject is highly susceptible to suggestion, oblivious to all else, and responds readily to the commands of the hypnotist.

neurosis. A psychological or behavioral disorder in which anxiety is the primary characteristic. Defense mechanisms or any of the phobias are the adjustive techniques which an individual learns in order to cope with this underlying anxiety.

psychoanalysis. A system of psychology directed toward the understanding, cure, and prevention of mental disorders.

Dr. Margaret Brenman-Gibson
General Questions

1. What is Dr. Brenman-Gibson's lifelong interest?

2. Who were her mentors and how did they aid her career?

3. What are the rewards of working in an academic setting?

4. How does Dr. Brenman-Gibson describe her marriage to writer William Gibson, and particularly what does she say about a marriage in which her career success came earlier than his?

5. What is a psychoanalytical biography? Why did she write such a biography of playwright Clifford Odets?

6. What stage does she note in discussing her life? For example, what became an acute issue at 35? How did she resolve this issue?

7. How does Dr. Brenman-Gibson evaluate her combining a career with being married and having two sons?

8. What are the possible short range and long range effects of Dr. Brenman-Gibson's political activism on her career?

Dr. Margaret Brenman-Gibson
Science Questions

1. What is hypnosis? How does it create an altered sense of consciousness? In addition to hypnosis, how can consciousness be altered? For example, how can psychopharmaceuticals be used?

2. How can science be used in studying something so seemingly elusive as creativity?

3. Dr. Karl Menninger, one of Dr. Brenman-Gibson's mentors, received his medical degree at Harvard Medical School. Later, he became clinical professor of psychiatry at the University of Kansas Medical School and chair of the board of the Menninger Foundation. Dr. Menninger is especially famous for his work on suicide. What are the advantages of a medical degree in the study of behavior? Might there be any disadvantages?

4. When studying human behavior, what problems, practical and ethical, arise in applying the scientific method?

5. What questions may arise in the use of psychopharmaceuticals?

6. What social issues arise from personal use of legal drugs like alcohol and of other illegal drugs, or from the abuse of controlled substances, in order to alter consciousness? Why are such drugs so popular?

7. Why conduct scientific inquiry into the nature of creativity?

Dr. Margaret Brenman-Gibson
Social Studies Questions

1. Do doctors and scientists have a special social or moral obligation to society? Dr. Brenman-Gibson's activism illustrates the nuclear issue. What other issues might be of concern?

2. What lessons in career development might be drawn from her life? Illustrate.

3. What challenges are presented to traditional sex roles during this interview? Explain. How do these challenges relate to you and your future?

4. Are a personal life and a family life compatible with an active and successful career in medicine? Explain.

5. What historical and social factors aided Dr. Brenman-Gibson's career development.

6. What does Dr. Brenman-Gibson mean when she says that "women have an infinitely more difficult role in life given the constraints on what they have been allowed to do over the centuries"?

7. Why has she made political activism on the nuclear arms issue one of her highest priorities? How does she reconcile an act of civil disobedience with her career? Do age and position influence this action?

Profile #8
SHIRLEY DRISCOLL, M.D.

BIOGRAPHY

Dr. Driscoll, a lucid and stimulating teacher, is also a committed mentor and supporter of Harvard's medical students and residents. As Director of Women's and Perinatal Pathology at the Brigham and Women's Hospital, she conducts research on various fetal diseases and inherited disorders. Her 1967 book, **Pathology of the Human Placenta**, is a classic in this field. In addition to her research, she discusses her medical school years and early marriage to a fellow medical student.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Pathologists

Residents in Pathology

Medical Equipment and Concepts Demonstrated:

Light Microscopy

Training Residents

Teaching Medical Students

Social Concepts Discussed:

Sharing Profession with Spouse

The Effect of the Women's Movement on Aspirations and Expectations

Decisions and Factors Affecting Career Advancement

The Significance of Collaboration in Scientific Research

Transcript

Interviewer: The Joint Committee on the Status of Women in conjunction with the office for Educational Programs has created and produced a series called "Women in Medicine" with senior women professors at Harvard Medical School. Today we're talking with Dr. Shirley Driscoll, Professor of Pathology at Harvard Medical School and Director of Women's and Perinatal Pathology at the Brigham and Women's Hospital.

Interviewer: Dr. Driscoll, where did you go to medical school?

Dr. Driscoll: I went to the University of Pennsylvania, Philadelphia.

Interviewer: And Dr. Driscoll, what influenced your choice of pediatric pathology?

Dr. Driscoll: Well, during medical school, the course in pathology, which was a second year course, was a wonderful course. It was wonderfully organized and taught. Furthermore, it was the first contact that we'd had with disease and that is very exciting for someone who wants to be a doctor, so they really had us at that point, they caught us at that point. So I thought I might be a pathologist, then, not very long after that, I attended a lecture by my professor of pediatrics who spoke more about the responsibilities and the opportunities involved in taking care of children with their whole lives ahead of them, in a sense, and that really touched something in me too. I thought somehow or other I would be either a pathologist or I would be a pediatrician. Then as time went on and I got more of my schooling and my training, I had to choose between those two possibilities and I decided that the youngest patients, which then I thought of as the newborns, would be, you know, sort of the epitomy of the challenge and opportunity of pediatrics. Also that there were many things to do about newborns, to understand a lot of their problems. Extending that to the fetus, the unborn, that I might be able to address their problems, either as a well trained pediatrician taking care of the youngest patients or as a well trained pathologist. Again as time went forward it seemed to me that pathology offered me more opportunity to do that. I had the good fortune to be able to find a setting in which I could pursue those interests and they extended to the consideration of pregnancy because I think that in a sense the factors in pregnancy have tremendous bearing on the quality of the prospective life of grown ups.

Interviewer: When did you meet your husband?

Dr. Driscoll: I met him on the first day of medical school, in the afternoon!

Interviewer: Did his friends become your friends?

Dr. Driscoll: Yes they did.

Interviewer: Was there sort of a comraderie, a sense of sharing with one another?

Dr. Driscoll: There really was, we were a couple in a sense from very early on, we started to see one another the first week of medical school, and formed a kind of nucleus of a group of mainly medical students, but students who were in other fields too who lived where my husband lived. He lived in a boarding house about which one could write a wonderful novel if one had the time because of the variety of people and their interests and some of the escapades that took place there! We were very actively involved in the life of that living unit.

Interviewer: Is it still in use?

Dr. Driscoll: It is in use, but it is out of print. If I were to do that book over again and if it were mine, rather than done in collaboration, and at the level of seniority that I have reached, I think I could make it a better book, not for content, but by being a little more judgmental, a little more evaluative in presentation of information. In a sense, sticking my neck out about certain phenomenon!

Interviewer: Much of your research relates to fetal development, in particular you were working on projects which examine the problems of diabetic pregnancy. Could you briefly describe your contribution to this research study?

Dr. Driscoll: Well, my first interest in this goes back a very long time. I would say probably to the early 50s when I became interested in the fact that women who are diabetics have less success in producing healthy surviving children than do their counterparts who are not diabetic. It was obvious that they had three or four areas in which their problems lay. One of them had to do with the fact that many of their babies had to be born prematurely and in such a setting they were at risk of having severe respiratory problems. Over time with the development of perinatal medicine, that problem has not been completely solved, but it is very close to solution. Another was that they tended to die before they were born for no known reason and that aspect has also lent itself to some preventive approaches that have been developed in perinatal medicine. There remained the problem of maldevelopment, that is the fetus or the embryo would have a malformed heart or a malformed brain or no kidneys, or something that would be disastrous or very handicapping if they were to be born alive. I wrote about that in the early 60s. I have been interested in characterizing, those would be descriptive things, and have taken every opportunity to work on that project which I, as a pathologist in the hospital setting, could work on. At the present time, we are one of the five institutions that are doing research with reference to malformation in offspring of diabetic mothers. I am the pathologist to the women's division arm of that project. Also, because we have an interest in early development, we are examining the products of miscarriage from diabetes in the process from two other centers, that is, at Cornell and Pittsburgh.

Interviewer: You said to me once, Dr. Driscoll, that a typical day in the life of Shirley Driscoll is an atypical day. Could you sort of describe how you spend your time in a day here at the hospital.

Dr. Driscoll: Every day I spend a substantial amount of my time being a hospital pathologist in a teaching setting in the subspecialty areas where I have established sufficient expertise. I may work with a microscope with residents, making diagnoses, I may look at slides, from uterine tumors, ovarian cysts, vaginal lumps, breasts masses to make diagnoses. That is, the patient has come in, had an operation, the tissue is ready for a diagnosis. We always do that in conjunction with someone in training so that we use the process toward two purposes, one to make the diagnosis and the second to teach, thus the feedback at that time is continuous. It's a big part of the day. I go to and participate in hospital conferences and there are many of those! It just depends on which week it is and what day it is. Committee work, dealing with projects that residents and other staff have undertaken. Reviewing papers that have been written, advising in that capacity. Reviewing policies, how we handle certain problems in the laboratory, going to medical school to teach.

Interviewer: Dr. Driscoll, you're known in particular for your enthusiasm about teaching. What specifically do you enjoy so much about teaching?

Dr. Driscoll: I think that what I am interested in, and science is terribly important, and I believe that I can communicate the challenges and importance of those subjects as a teacher.

Interviewer: Did that make you feel any less isolated as a woman?

Dr. Driscoll: I think it did. I don't think that the group did, as much as the fact that he and I would spend so much time together.

Interviewer: Could you briefly describe your residency training, in particular how you seemed to alternate it with your husband's residency training.

Dr. Driscoll: Yes, my husband and I were classmates. We had financial problems and we were not sure what fields we wanted to be in, but each of us wanted the other to make choices and to be able to pursue his or her interests. Having such limited financial resources, we had to make some kind of an agreement that while one worked to support us, the other one could study and vice versa. That was the sort of general spirit of our planning, and then certain other factors bore on where we went and how things evolved including the fact that he was in the Air Force for a couple of years and I wanted to be near where he was while trying to do something that would have good medical content, would be satisfying and I would hope would be educational. Gradually we meandered along the road together and ended up trained in our fields.

Interviewer: I would like to talk briefly now about your research career. Is there one piece of work in your career that has been perhaps exceptional in attracting people to you, that you would look to as your major work?

Dr. Driscoll: That is very difficult to answer. I think that probably my interest in the placenta has a broad sort of focus, if that is not a contradictory statement. The fact that I have been interested in the placenta and the fetus have been more a distinction for me than any other of my interests.

Interviewer: Could you describe the impact of your book, **The Pathology of the Human Placenta**.

Dr. Driscoll: At the time we wrote the book, there was a perceived need, on the part mainly of people who were in obstetrics and some people in pathology, for a volume that would gather together information from widespread sources on this particular topic. There was a need to do that, to provide kind of an authoritative compendium of the information that could be used by the pathologist and applied in a sense to clinical problems, to sort of point the way and I think that that is where the book has had its greatest influence.

Interviewer: It was published, I believe in 1967.

Dr. Driscoll: '67, that means it was complete in '65 which is a long time ago.

Dr. Shirley Driscoll
General Questions

1. Dr. Driscoll and her husband were in medical school and residency training at the same time. What was unique about this period in their lives?

2. Dr. Driscoll wrote a book, **The Pathology of the Human Placenta**, that was published in 1967. What advantages in writing the book would she have now, over what she had in 1967? Why?

3. Why does Dr. Driscoll feel that her role as a teacher is so important? How are knowledge and experience passed on to others?

4. Why did Dr. Driscoll become a pediatric pathologist? What factors influenced Dr. Driscoll's choice to become a pediatric pathologist?

5. What role has marriage played in Dr. Driscoll's career? How did the couple accommodate two medical careers, hers and Dr. John Driscoll's as an obstetrician?

6. Why does she describe her typical day as "atypical"? What tasks does she perform?

7. What personal traits does Dr. Driscoll reveal through her career?

8. What is shown about planning and decision in a career?

Dr. Shirley Driscoll
Science Questions

1. What is involved in the study of pathology?

2. What was the major medical work of Dr. Driscoll?

3. Dr. Driscoll is currently doing research which involves investigating problems associated with diabetic pregnancies. What are some of the problems that develop in the fetus, with a maternal diabetic environment?

4. How does Dr. Driscoll's work illustrate the connection between basic and applied research?

5. What advantages do you see associated with the acquisition of new knowledge in the area of fetal development?

6. How might new information associated with tissue differentiation and morphogenesis lead to treatments of abnormal tissue/organ development? Do you feel the fetus can and should be treated as a patient?

7. Currently, there are five institutions involved with research on malformation in offspring of diabetic mothers. What are the advantages associated with several facilities doing the same work? What could be a potential problem? Why?

Dr. Shirley Driscoll
Vocabulary

diabetes. A metabolic disease in which carbohydrate utilization is reduced and that of lipid and protein is enhanced. It is caused by a deficiency of insulin.

morphogenesis. The differentiation of cells and tissues in the early embryo which results in establishing the form and structure of the various organs and parts of the body.

pathology. The medical science, and specialty practice, that deals with all aspects of disease, but with special reference to the essential nature, the causes, and development of abnormal conditions and disease processes.

perinatal medicine. The branch of medical science dealing with care and treatment before, during, or after the time of birth.

placenta. The organ of metabolic interchange between fetus and mother. The human placenta, at term averages about 1/6 to 1/7 the weight of the fetus, and surrounds the fetus until birth.

tissue differentiation. The acquisition of specialized function and character of collections of similar cells and the intercellular substances surrounding them.

Dr. Shirley Driscoll
Social Studies Questions

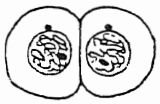
1. How does Dr. Driscoll's work show that research is a "social process"?

2. How are knowledge and experience passed on to others? How do Dr. Driscoll's experiences show that medicine is a highly "social process"?

3. Describe Dr. Driscoll as a role model for young people. What might you incorporate as part of your own self?

4. What dilemmas might confront a couple when both have careers in medicine?

5. What does Dr. Driscoll's life and work say about aging and creativity?



Profile #9
PRISCILLA SCHAFFER, Ph.D.
Professor of Microbiology and Molecular Genetics

BIOGRAPHY

One of America's leading virologists, Dr. Schaffer attributes her very early success to hard work, ambition and a willingness to take risks. Dr. Schaffer is Chief of the Laboratory of Tumor Virus Genetics at the Sidney Farber Cancer Institute, where her major research is concentrated on defining the DNA of the **Herpes Simplex** virus. Dr. Schaffer's commitment to improving medical education began during her early years at Baylor University; as a member of the Admission Committee at Harvard Medical School, she is a strong supporter of women and minority students.

VIDEOTAPE SUMMARY

Professionals Portrayed:

Virologists

Research Scientists — (Ph.D.s) — post-Doctoral Fellows

Laboratory Technicians

Medical Equipment and Procedures Demonstrated:

Tissue Culture Techniques

Electrophoresis of Proteins

Glycoprotein Analysis

Social Concepts Discussed:

The Significance of Mentors in Career Development

The Importance of Collaboration in Scientific Research

The Effects of the Women's Movement on Aspirations and Expectations

Decisions and Factors Affecting Career Advancement

Updating Medical Education

Transcript

Dr. Schaffer: One of the most common questions that I'm asked by the candidates for Harvard Medical School, the females, the women, is "what's it like to be a woman at Harvard?"

Interviewer: The Joint Committee on the Status of Women has created and produced this series on "Women in Medicine" with senior women professors of Harvard Medical School. Today we're talking with Dr. Priscilla Schaffer, Professor of Microbiology and Molecular Genetics.

Dr. Schaffer: I literally fell into a project that has been my life's work. The problem, as you know, involves **Herpes simplex** virus and specifically the genetics of **Herpes simplex** virus and how the virus transforms cells. In fact, we and others have shown that one specific piece of this viral DNA is able to transform cells. So that now we can focus our attention on using this genetic approach on that piece of DNA, and we can say what genes specifically are present in that small piece of DNA which now represents about 15% of the genome, having eliminated 85% of the genome. Indeed, it seems that there are about 7 genes and our current efforts are focusing on identifying the specific functions which each of those genes performs, again during the active infection initially. Then later on, and concurrently actually, we're asking what are the functions of these gene products in transformation? I can say that we know something rather specific about three of those seven genes.

The first gene is the gene for a glycoprotein which is called GAGB and this glycoprotein has been shown to be essential for the penetration of virus particles into cells because the glycoprotein is present on the surfaces of virus particles and if this glycoprotein is defective in some way as in the case of some of our mutants or if it's absent then the virus particles can attach to cells but it won't cut in, it won't penetrate.

The second gene about which we know a fair amount is the gene for the major viral gene binding protein viruses make in cells and this particular protein has the ability to unwind the DNA and perhaps facilitate transcription or DNA replication. So that we know something about what this protein is doing in productively infected cells. The question is, do we find it in transformed cells? The answer is, yes we do. It certainly is in transformed cells and what is its role in transformation? We are not certain, but it is interesting that this protein is found in about 40% of cervical carcinoma biopsy specimens and we have shown that in fact the degree to which this protein is expressed, now I am talking about cells transformed in laboratory, **in vitro**. The more of the protein that is present in those cells, the more cells that have the protein, the more tumorgenic the cells will be in newborn animals. So that there seems to be a correlation between the expression of this protein and tumorgenicity, at least in the laboratory.

And the last gene about which we know something is the gene for viral DNA polymerase, the **Herpes Simplex** virus specifies its own viral DNA polymerase, it doesn't use the polymerase of the cells which many DNA viruses do. Interestingly, Don Cohen in my lab, a post-doc, in collaboration with Jennifer Hall of the University of Arizona have shown that this viral DNA polymerase, interestly, is a mutagenic polymerase. In other words, it is not a very faithful copier of DNA. Others have shown that in addition to the polymerase function, there is an exonuclease function associated with the protein. One could postulate that a potential mechanism of transformation would be if this polymerase found itself in a cell and it is able to, if the nuclease function was able to act on the cellular DNA, for example, and also the protein had unfaithful copying properties. This could possibly be responsible for mutagenesis of cellular DNA. The mechanisms which we propose, and others propose, for the action of the polymerase is called the "hit and run" hypothesis because one only needs, in both the presence and the polymerase, one would have to have the viral DNA present for some time, sufficient time for viral DNA polymerase to be made. The polymerase is made, it acts on the cellular DNA mutagenizing it, some manner of it and then the viral DNA can disappear and the polymerase in fact can disappear. This is in fact consistent with the finding that in **Herpes simplex** virus transformed cells one is often hard put to demonstrate the presence of viral DNA or viral proteins, you can find them early after transformation, the DNA is present, you can find viral proteins yet the cells are transformed. So at least the observation that we can't find DNA in proteins is consistent with this "hit and run" hypothesis and specifically, the people in my laboratory are working on problems associated with the three genes I mentioned.

Interviewer: What types of problems are the people in your lab working on?

Dr. Schaffer: Yes, Dr. Cohen, a post-doc who has recently been appointed assistant professor in the Department of Pharmacology here at Harvard Medical School, has been working on the polymerase, the properties of polymerase, trying to identify the sites of activity, polymerizing activity and to map it on the viral genome. He is also interested in the fact that the **Herpex Simplex** viral DNA polymerase is a locus, which when mutated can confer resistance to some of the most important anti-herpes drugs.

Dr. Weller, another post-doctoral fellow, is studying the major DNA binding proteins and she is also interested in introducing mutations, new mutations into this piece of DNA hoping to identify any additional genes that may be present. You simply, in this case, isolate the fragment of DNA and mutagenize it in vitro, and there are ways in which we can reintroduce this mutagenized piece of DNA into the normal virus and then ask, "What has our mutation done, and can we identify a new gene for example in that piece of DNA?" So she is interested in nucleic acid biochemistry as well and is involved in cloning and mapping mutations, fine structurally, that we know are present in the morphologic transforming region.

Dr. Saboren is the person who has most recently been involved directly in the transformation studies, that is, attempting to transform cells with ever smaller pieces of DNA to try to identify the minimal piece of DNA that will transform cells. He also looks in cells, that are transformed by the virus, for the presence of these viral proteins, the glycoproteins, GAGB, DNA binding protein, hopefully, ultimately the polymerase, although there is no ready assay in transformed cells for the presence of the polymerase, we hope to be able to develop one.

Dr. Betty Pancake and Dr. Richard Respess, two fellows, are working on the glycoprotein specified by the virus, the reason that we are interested in the glycoproteins is not only because glycoprotein GAGB is involved in transformation, of course we would like to know as much as we can about that glycoprotein, but I mentioned before that the immune response somehow plays a role in maintaining the latent infection. The latency is clearly a problem for us, it is fine for the virus, but we are interested then in knowing how does the immune response play a role in maintaining latency. In order to do this we have to know something about the immune response and we do know that the viral glycoproteins are the major antigens which stimulate the immune response. So these two post docs are involved in identifying the viral glycoproteins that the virus makes. We are now in the process of using mutants which don't make individual glycoproteins. They make everything but this glycoprotein, everything but another glycoprotein. We are asking, what is the nature of immune response to a virus like that, for example; have we impaired the cellular immune response; is there less of a humoral immune response; and can the virus then become latent in an animal which has a certain kind of antibody, or a certain kind of cellular immune response? So these are the kinds of problems that we are working on.

Interviewer: What exactly were the enticements of coming to Sidney Farber?

Dr. Schaffer: There were times, especially later during my stay at Baylor when I felt that I needed to grow and that the place no longer, the lab, at least that lab no longer offered the kinds of things that I wanted for myself, and that was mostly independence and so after six years I decided that "I am going to look for another position." I had an opportunity to work with another very well known herpes virologist but decided against it because I would have, I felt, gone from the shadow of one mountain to the shadow of another and I really wanted to build my own mountain!

Interviewer: How did you go about looking for a new job at this stage?

Dr. Schaffer: Well I, fortunately, I didn't really look for a new job. I was giving a paper in Nuremberg on my studies, the studies of my group, and Jack Strominger, who was then putting together a new group at the Farber asked me if I would be interested in coming to the Sidney Farber and I said yes. So with the financial situation at Baylor and my dissatisfaction with that part of my professional life and this good opportunity, and also I had been asked by Bernard Risman at the University of Chicago whether I would be interested in coming to his laboratory, I felt very strongly that now was the time for me to go. As I have indicated, Dr. Risman is a herpes virologist and he was the mountain whose shadow I wished not to be in, so I came here instead. Of course, the decision was based, well, on the tremendous research opportunities here, marvelous intellectual environment and the fact that one can get good post-docs and graduate students here and in other places it is somewhat more difficult. So there were many opportunities I felt that Harvard offered and also the position here was one of full independence and that was very appealing.

Interviewer: Is it curious to you that there are three women professors in this department?

Dr. Schaffer: I think it is fantastic of course, but again, it doesn't surprise me in that I mentioned before Microbiology has always been very kind to women, very appreciative. I think that other departments at the school should follow the lead of Microbiology and I've heard some pretty sad excuses why there aren't more tenured women in other basic science departments and the clinical departments as well.

One of the most common questions that I am asked by the candidates for Harvard Medical School, the females, is, "what is it like to be a woman at Harvard," and I think that this is a rather serious problem. I think that perhaps it is less serious for the younger people, the women who are with each other in classes, than it is for a young assistant professor, for example, or an associate professor, because the higher you get the more isolated you are, that's part of the deal. I can't say that I feel terribly isolated in a sense that my male colleagues are my good friends and so forth. That's fine, but there are problems that are unique to women and I think that it would be in numerous instances I can think of, times when I would like to have been able to speak with a female colleague of the same faculty rank and I look around and I say, you know there just isn't anyone.

Interviewer: You have, in a sense, made it to the top at a relatively young age. What are the costs of success?

Dr. Schaffer: Well, I don't know that there have been any, let's just say I have no regrets. I don't think I have paid anything that I have second thoughts about. The cost has not been that great; I think the benefits are greater than the costs. I think some of the disadvantages of which I am aware are probably social in that I haven't taken the time to enjoy life socially as much as some other people might have, some other women might have. Family, that is something that perhaps I would have considered.

Interviewer: Did you make a conscious decision not to have a family in deference to your science.

Dr. Schaffer: Actually I did. This was in college, graduate school. I don't think that it can't be done, I think it can be done. I just know myself, that I am very ambitious, or certainly was then, and that in order to have a family and to give to children the quantity and quality of attention that I think they need, that I wasn't willing to make that commitment and that was actually a conscious decision.

Interviewer: You were involved in the Admissions Committee at which time you had contact with prospective students, which encouraged you to be interested in curriculum. Do you have any comments about the curriculum?

Dr. Schaffer: Well, yes I have some rather strong feelings about the curriculum. I was also involved in the curriculum matters at Baylor and also at Cornell even as a graduate student. I have taught medical students for a long time and I am somewhat concerned that curriculum reform here has revolved more around the desire and the needs of department chairmen than around those of the medical students themselves. I know that this is a question which many prospective students ask when they come here, they, of course, have heard that there is some reshuffling of the curriculum going on. I know that the faculty, many of them, are not pleased with the situation and of course we know now that there is a move afoot to rethink the whole curriculum concept here at the school. I think it is great.

biochemistry. Physiological chemistry; biological chemistry; the chemistry of living organisms and of the changes occurring therein.

biopsy. The process of removing tissue from living patients for diagnostic examination.

cancer. A general term frequently used to indicate any of various types of malignant neoplasms, most of which invade surrounding tissues, may metastasize to several sites, and are likely to recur after attempted removal and to cause death of the patient unless adequately treated.

cellular immune response. The cell-mediated mechanism whereby tissue previously sensitized to an antigen tends to resist infection; **or** the response of that mechanism that produces the initial sensitization to an antigen.

cervical carcinoma. A malignant neoplasm derived from epithelial tissue in the uterine cervix.

chloroplast. A plant cell inclusion body containing chlorophyll; occurs in cells of leaves and young stems.

chromosome. One of the bodies (normally totally 46 in humans) in the cell nucleus that is the bearer of genes; it has the form of a delicate chromatin filament during interphase, contracts to form a compact cylinder segmented into two arms by the centromere during metaphase and anaphase stages of cell division, and is capable of reproducing its physical and chemical structure through successive cell divisions.

cytogeneticist. A specialist in cytogenetics, the branch of genetics concerned with the structure and function of the cell, especially the chromosomes.

DNA. Abbreviation for dioxyribonucleic acid.

DNA methylation. The addition of a methyl group to DNA.

DNA polymerase. Enzyymes (transferases) transferring nucleotide residues (nucleotidyls) from nucleoside di- or tri-phosphates into dimer or polymer forms.

DNA replication. The process by which DNA in chromsomes replicates or produces exact copies of itself.

enzyme. A protein, secreted by cells, that acts as a catalyst to induce chemical changes in other substances, itself remaining apparently unchanged by the process.

exonuclease. A nuclease that releases one nucleotide at a time, serially, beginning at one end of a polynucleotide (nucleic acid).

gene. The functional unit of heredity. Each gene occupies a specific place or locus on a chromosome, is capable of reproducing itself exactly at each cell division, and is capable of directing the formation of an enzyme or other protein.

genome. The genes in the complete set of chromosomes derived from one parent, the haploid number of chromosomes.

Herpes simplex virus. The pathogen of **herpes simplex** in people causing acute stomatitis, especially in children, and so-called fever blisters, usually on the lips and external nares.

humoral immune response. The antibody-producing mechanism of response to an antigen associated with the extracellular fluids of the body: blood and lymph; in contradistinction to **cellular** immune response, as originally proposed in Metchnikoff's phagocytic theory.

leukemia. Disease of progressive proliferation of abnormal leukocytes found in hemopoietic tissues, other organs, and usually in the blood in increased numbers.

locus. A place; usually, a specific site.

methyl group. A group of the radical, $--CH_3$, present in a variety of compounds.

morphology. The science which deals with the configuration or the structure of animals and plants.

mutagenesis. The production of a mutation.

mutant. An individual possessing one or more genes that have undergone mutation, that is, a change in the character of a gene that is perpetuated in subsequent divisions of the cell in which it occurs.

protein. Macromolecules consisting of long sequences of alpha-amino acids in peptide linkage. Protein is three-fourths of the dry weight of most cell matter, and various proteins are involved in structure, hormones, enzymes, muscle contraction, immunological responses, and other essential life functions.

recombinant DNA. DNA produced by recombination or crossing-over between two homologous chromosomes; associated with the increased production of proteins — for example, interferon.

tumorgenecity. The quality of causing or producing tumors.

Dr. Priscilla Schaffer
General Questions

1. How does Dr. Schaffer answer those who ask "What is it like to be a woman at Harvard?" Why does she see this as "a rather serious problem"?

2. What conscious decisions did Dr. Schaffer make about a family? When? Why?

3. What personality traits does Dr. Schaffer reveal? How were they helpful in establishing a successful career in scientific research?

4. What does the interview show about running a research laboratory?

5. Why did Dr. Schaffer come to Sidney Farber Cancer Institute?

6. What does Dr. Schaffer mean when she says "I really wanted to build my own mountain"?

7. What factors did she consider when she decided to look for a new position? Why did she feel that "now was the time for me to go"?

8. Why do women in medicine have to deal with isolation in their careers? How can this isolation be overcome? Who is responsible for bringing about this change? Why?

9. What do people mean when they say "my life's work"? Do you see yourself as having a single "life's work" or as having a number of jobs or careers? What social and economic factors influence these answers?

10. What responsibility do industry, private foundations, and individuals have to support basic and applied medical research?

11. What were some of the trade-offs that Dr. Schaffer had to make, as she rose through the medical school ranks? Do you feel that these were reasonable trade-offs?

Dr. Priscilla Schaffer
Science Questions

1. The research interest of Dr. Schaffer involves the molecular genetics of **Herpes simplex** virus. What is the key question asked by Dr. Schaffer, as it concerns the interaction of virus with host cell?

2. Dr. Schaffer and her medical team have isolated a section of viral DNA which represents about 15% of the viral genetic information. It appears that this "bit" of DNA consists of about 7 genes. What are the reasons for determining the products of these genes?

3. What was the relationship that was established between the quantity of viral gene binding protein and the degree of tumorgenecity in animal cells?

4. What is meant by the proposed mechanism known as the "hit and run" hypothesis?

5. Why is it so difficult to establish a cause and effect relationship between viral interaction with host cells into tumor cells?

6. It has been identified that the gene for DNA polymerase is a locus, that when mutated can confer resistance to some of the most important anti-Herpes drugs. What is the significance of this relationship?

7. What is a potential result of a mutation of the gene that codes for DNA polymerase in **Herpes simplex**?

8. The host's immune response appears to play a negative role, as it relates to the herpes simplex virus. What is this relationship? What is the significance of this relationship?

9. What are the major viral antigens which stimulate the host's immune response?

10. Dr. Schaffer's work with **Herpes simplex** is in basic research. However, why is this basic research of interest to the public? How do public interests influence trends and funding in basic research?

11. What do you see as real dilemmas in trying to link a specific virus to cancer? Why are correlation studies that demonstrate the presence of a virus within a host cell somewhat misleading?

12. How important is the sharing of information between separate lab teams investigating the same topic? Do you feel that it is common practice without a second thought? Might there be reasons why a particular lab team might not share acquired information? If so, what would these instances be?

13. It has been established that certain gene loci can mutate. These mutations can confer resistance to some of the most important anti-herpes drugs. What is the significance of this type of mutation? Why does this create a problem with the treatment of diseases caused by the **Herpes simplex** group?

Dr. Priscilla Schaffer
Social Studies Questions

1. Dr. Huang decided on having a child and still maintaining the same level of her career. Dr. Schaffer opted for not having a family because one could not maintain the intensity of a demanding career and still give the child the quantity and quality of attention. How do you feel about the dilemma of integrating a demanding career in academic medicine with raising a family?

2. How does Dr. Schaffer's career challenge stereotypes? Explain.

3. Ideally, at what level should the federal and state governments fund basic and applied medical research? Where would you place funding of medical research on a list of national priorities? What would be the long and short range effects if government funding for medical research was increased?

BIOGRAPHICAL INFORMATION:

Linda H. Brink, Ph.D.
Executive Producer

Linda H. Brink, Ph.D., is a biochemist/immunologist with joint appointments in the Department of Pathology, Harvard Medical School and Human Development, Harvard Graduate School of Education, Boston, As the principal investigator of research projects studying the effector mechanisms of schistosome immunity, Dr. Brink has isolated and characterized several **Schistosoma mansoni** antigens which are being tested in pre-vaccine trials.

Dr. Brink also created and produced an on-going series of videotaped oral histories of senior scientists, **Workers In Tropical Medicine,** sponsored by the National Library of Medicine and the American Society of Tropical Medicine and Hygiene. Dr. Brink has presented her research on role models and mentor relationships in academics at numerous conferences and colleges.

Geri Denterlein
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Geri Denterlein, former Acting Director of Harvard's Office for Academic Careers, is a communications specialist with experience in both the health/science and political arenas. As Forum Program Coordinator at Harvard's Kennedy School of Government, Ms. Denterlein produced public events of a political nature for presentation on a near daily basis. Television production experience includes work on "The Advocates" (PBS), "Miller's Court" (WCVB), and on-camera host of **Health Exchange** (Warner Amex). She is currently Director of Public Affairs, Department of Mental Health, Commonwealth of Massachusetts.

Joy Wallace
Editor
Women In Medicine Guide

Joy Wallace, Educational Consultant and Project Director for EQUALS: New England, is an experienced trainer and materials developer. She has a national reputation in the area of sex equity in education. She has published materials on Affirmative Action, implementing change in education, equity issues in computer education and assessing equity in teacher attitudes and actions. She is currently working as an independent consultant in New England.

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