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?