



Janet Ward McArthur



Janet Ward McArthur was born in Bellingham, WA on June 25, 1914 and died at the age of 92 among friends at North Hill, Needham MA, on October 6, 2006.

She obtained her AB degree, *magna cum laude*, at the University of Washington in 1935, her MD at Northwestern University Medical School in 1942, and, after internship and residency at Cincinnati General Hospital, became a resident in medicine at MGH in 1945. She then became an HMS Research Fellow, and, successively, an Instructor in Pediatrics and an Instructor in Gynecology at MGH. She was a member of the Thyroid Clinic at MGH 1945 - 1952.

A list of Dr. McArthur's achievements attached to a picture of her in a celebration of distinguished women in medicine at MGH includes:

- (1) a method of measuring LH, and identifying the midcycle peak;
- (2) increased LH and FSH in non-menstruating and postmenopausal women;
- (3) the fact that the cervical mucus of the bonnet monkey (macaque) facilitates the transport of sperm to the uterus and tubes;
- (4) the effect of stress, diet, and exercise on the menstrual cycle.

Her bibliography of 129 papers and two books begins with the first paper in 1939, and a last one in 1999. Of these, she was the first author of 30 papers.

John Stanbury in his history of the MGH Thyroid Clinic and Laboratory, 1913 - 1990, entitled "A Constant Ferment", describes Dr. McArthur: "a quiet but assertive and hugely competent physician, she more than held her own in a professional environment that was male-dominated. She participated in anti-thyroid drugs, thyroid tumors, and clinical applications of radio-iodine. One of her important studies was a review

of the clinic's experience with thyroid storm. With Cope and Rawson she described the hyperfunctioning single nodule, which might or might not produce thyrotoxicosis".

(That definitive article is to be found in Surgery, Gynecology and Obstetrics 84: 415-126, 1947).

In 1952 she was co-author of N. B. Talbot's book, "Functional Endocrinology from Birth through Adolescence".

In 1954 she was first author of 2 papers, with 14 coauthors on the first and 11 on the second, which showed in experiments on diabetic dogs that stress or ACTH administration, and not only insulin deprivation, could cause acidosis.

Her many important studies on gonadotropins began with a 1952 paper, with herself as sole author, on pituitary LH in the urine of young women, measured by Greep's bioassay, the response of the ventral prostate of hypophysectomized rats. This and subsequent papers employed bioassays for measuring gonadotropins: the Greep assay, and the Steelman-Pohley (ovarian weight increase after HCG), or a testicular weight assay, for FSH.

In 1958, studying normal men and women of various ages, she found LH to be undetectable in prepubertals, while in normal adult women there was a 2-to-4 fold midcycle peak, indicating ovulation, a trough, and a slight increase premenstrually. In 1959 she described LH abnormalities in longitudinal studies of women with polycystic ovary (Stein-Leventhal) syndrome.

In 1961, the year that marks the beginning use of oral contraceptives combining estrogen and progestin (mestranol and norethynodrel) Dr. McArthur showed that estrogen administered to women during the follicular phase postponed the normal midcycle peak of LH while progesterone administered alone was of no effect.

She was familiar with the high levels of FSH and LH in postmenopausal women when, in 1964, she studied subfractions of postmenopausal plasma prepared by the Cohn method in comparison with a preparation from postmenopausal urine.

In 1971 she began studies of the cervical mucus of the bonnet monkey, its anatomical basis and physiological regulation, recognizing its importance in the transport of sperm to the uterus and tubes. In a subsequent study, viscosity changes and increased sialic acid concentrations were confirmatory.

In 1972, Dr. McArthur became the first woman at MGH to be accorded full Professorship at HMS, as Professor of Obstetrics, Gynecology and Reproductive Biology.

In 1974, a key article by Rose Frisch and Dr. McArthur in "Science" reviewed the literature on resumption of menses in undernourished lactating women and the measurements obtained by Frisch in 7

prior studies of menarche and critical weight in 181 girls. The article provided a mathematical analysis of fatness as a determinant of the critical weight-for-height necessary for the onset and maintenance of the menstrual cycles. The study included the estimate that the stored fat provided the 144,000 calories of easily mobilized energy necessary for pregnancy and lactation.

In 1976 Dr. McArthur felt that it was time to speak up about the status of women scientists in the Endocrine Society. Her friends suppressed their amusement when this small figure of a woman confronted a plenary session of scientists with an intentionally plodding parody of a scientific presentation, demonstrating in successive slides that the number of women who were members, or on committees, or chairing sessions, or editing manuscripts for journals, and so on, was vanishingly small. As a result, together with Drs Eugenia Rosemberg, Anne Carter, Neena Schwartz and others, Women in Endocrinology (WE) was formed to promote and facilitate professional development and advancement of women in the field of endocrinology.

In 1977 Dr. McArthur received the titles of Gynecologist at M.G.H. and co-Director of the Vincent Memorial Laboratory.

In 1981, again with Dr. Rose Frisch, Dr. McArthur compared postpartum amenorrhea with that associated with stress and analyzed data that compared the endocrine effects of exercise/training in pre-menarcheal as opposed to post-menarcheal young women. The data showed that each year of training before menarche delayed it by five months beyond the normal menarcheal age.

By 1976 Dr. McArthur had participated in writing 42 papers. She was first author of 15 of these, including the two papers on diabetes in 1954, already mentioned, which had 14 and 11 coauthors, and the 1964 paper on Cohn fractions of plasma, which had 5 coauthors. These, together with the 1970 book with T. Colton, a compendium of many scholars on statistics in endocrinology, are a small sample of Dr. McArthur's ability to be central to an effective research group.

In 1973 Dr. Inese Z. Beitins joined Dr. McArthur's research team. (Subsequently Dr. Beitins has been, successively, Professor of Pediatrics and Communicable Diseases and Director of the Division of Pediatric Endocrinology at the University of Michigan, Director of Clinical Research at the National Center for Research Resources at NIH, and Senior Consultant to the Director of the Office for Human Research Protection.)

In 1976 Dr. McArthur and Dr. Beitins worked with Dr. Maria Dufau at NIH, mastering the technology of radioimmunoassay (RIA) for the measurement of the gonadotropins, LH and FSH, their subunits, and other polypeptides as well as steroids. With this technology, together with a new in vitro bioassay for LH based on testosterone production by rat Leydig cells, they were able on their return to compare LH levels both by bioassay and RIA in both sexes and in a variety of circumstances including stimulation by GnRH (gonadotropin hormone releasing hormone), and to examine biological to immunological (B:I)

activity ratios. The data suggested that in women higher B:I ratios accompanied states of increased biosynthesis and release of gonadotropins. A later study found no change over time in B:I of men.

At the same time, they explored the effects of stress, fasting, severe dietary restriction and strenuous exercise on the pituitary-gonadal axis in men and women. By the time Dr. Beitins left MGH in 1983, she had collaborated with Dr. McArthur on 26 papers. The last, published in 1991, demonstrated two types of luteal dysfunction caused by the rapid initiation of strenuous exercise in young women.

Not long after the arrival of Dr. Beitins, Dr. McArthur was joined by younger associates beginning significant careers. Among these, in chronological order, were Dr. William F. Crowley, now Director of Clinical Research at MGH and Professor of Medicine at HMS, Dr. Thomas H. Badger, now Director of the Arkansas Nutrition Center and Professor of Pediatrics and Physiology at University of Arkansas Medical School, and Dr. Anne Klibanski, later the first Director of MGH's Neuroendocrine Unit, and now Professor of Medicine at HMS.

Several noteworthy contributions emerged from the time they spent with Dr. McArthur:

Dr. Crowley examined the effect of administration of a potent GnRH (gonadotropin releasing hormone) analogue to hypogonadotropic male patients who, unlike normal males, had failed to exhibit normal GnRH secretion at puberty. Later studies showed that the hypogonadotropic subjects responded paradoxically to the GnRH agonist, administered repeatedly, with decreasing LH secretion. This effect could then be applied to the treatment of children with central precocious puberty, and more recently, to prostate cancer, endometriosis, and uterine fibroids.

Drs. Beitins and Badger studied amenorrheic track athletes, finding low to normal levels of FSH and LH, normal LH pulse frequency, and normal to increased response to GnRH. Their studies of fasting and refeeding postmenopausal women suggested that carbohydrate administration reduced gonadotropinuria as a result of reduced renal excretion of ketones, including glycoprotein hormones.

Dr. Klibanski found that young women with hyperprolactinemic amenorrhea developed bone loss, and showed that acquired GnRH deficiency leading to estrogen deficiency in such women led to increased risk of osteoporosis. These studies opened up the area of neuroendocrine regulation of bone mass.

Dr. Beverly Bullen, a nutritionist at Boston University, became an important co-worker in 1981 with a first paper on melatonin increasing with exercise in women, followed by a total of eleven papers ending in 1999. Two of these were about melatonin and eight were concerned with permutations of the effects of strenuous exercise on hormone secretions.

In 1982 Dr. McArthur became an Adjunct Professor at Boston University. On reaching the age of 70 in 1984, she became Emeritus at HMS. She retired from the Vincent Laboratory and worked for three years at St. Bartholomew's Hospital in London, writing a single-author paper on the increased secretion

of beta-endorphins and beta-lipoprotein in exercising women. After that she joined Dr. Bullen in working at Boston University's Sargent College of Allied Health Professions.

Dr. McArthur was an intrepid traveler, enduring the fierce cold of the Himalayas at the age of 65 and being the only one in her party who did not suffer from altitude sickness. Later, with Dr. Bullen, she enjoyed the penguins of the Weddell Sea, and last of all, the polar bears of Manitoba.

Dr. Bullen noted that Dr. McArthur "had a very strong work ethic and was a very modest person who didn't like to attract attention to herself. One would never know from her what a pioneer she had been".

Dr. McArthur's patients adored her, as their subsequent caretakers have learned.

The memory of her achievements, her knowledge, her depth of involvement – her soul – is secure with all for whom she was a caring physician, all who worked with her, all who knew her, and all who have come to know her through study and reflection.

Respectfully submitted,

George S. Richardson, *Chair*

Fredric D. Frigoletto, Jr.

Isaac Schiff

Beverly A. Bullen