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DWIGHT JOYCE INGLE

1907—1978

A Biographical Memoir by
MAURICE B. VISSCHER

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Biographical Memoir

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Dwight J. Engle

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September 4, 1907–July 28, 1978

BY MAURICE B. VISSCHER

IT IS DIFFICULT to compress into a memoir of reasonable length the story of a scientist who was born on an Idaho ranch, educated in an ungraded elementary school and small town high school, attended a newly established state university, and yet went on to become a first-rank, pioneering scientist in a new and uncharted field. Yet even from this short account it will be apparent that his life was of importance to the advancement, philosophy, and ethics of science.

The period of Dwight Ingle's active life was the time of rapid development in endocrine science, to which Ingle himself contributed greatly. His career included a series of statistically improbable successful ventures, chronicled in his autobiography, *I Went to See the Elephant*.¹ The title comes from John Godfrey Saxe's story of "the six blind men of Indostan," who describe an elephant according to the part of the animal they can touch with their hands, and Ingle displayed genuine modesty in choosing it, for, as he explains in the book's preface, "Science does involve looking at some specific properties of systems that are too big to get into perspective." With a simple and genuine modesty, he continues:

This may be the first time that a non-famous scientist has written an autobiography. I hope it will show that an ordinary fellow can have fun being a scientist. There has been some self-direction in my life, but it may well be that the origin of some of my drives and faiths are hidden. Fortuity has played an important role in determining my interest, opportunities, and what has become of me.¹

EDUCATION AND EARLY LIFE

Dwight Joyce Ingle was born September 4, 1907, on a ranch near Kendrick, Idaho. He attended a small country elementary school and graduated from high school in Kendrick. At eighteen he entered the University of Idaho with a career as a physical education director in mind. Interested in weightlifting and wrestling since he was a boy, he had not yet acquired any real interest in science though he was a voracious reader. This situation changed very soon under the influence of the faculty.

Ingle's first serious scientific interest was in the field of psychology, which perhaps intrigued him because he engaged in summer work in state mental hospitals in Idaho. As he tells the story in his autobiography, he soon became disillusioned with the treatment and methods of care then available for the mentally ill, coming early to the conclusion that psychoses are organic illnesses. His interests, therefore, shifted to physiological psychology. Earning the Bachelor of Science degree at the University of Idaho in 1929, he enrolled there as a graduate student and earned a Master's degree in psychology in 1931. During his years at the University of Idaho, Ingle began reading the literature of endocrinology and studying adrenalectomized animals. He supported himself as a graduate student by working part time as a laboratory animal caretaker and by grading examination papers.

The Great Depression was then under way in the United States, and life was hard for most graduate students. Ingle was offered a small stipend as a teaching assistant at the Uni-

versity of Minnesota that allowed him to continue his graduate studies. He knew of Karl Lashley and others' basic work in physiological psychology at Minnesota and planned to emulate them. As it happened, however, his interests and his work shifted from psychology to fundamental endocrinology.

The author of this memoir was a member of the University of Minnesota Graduate School Committee that conducted Dwight Ingle's final examinations for the Ph.D. degree. He had majored in psychology and minored in physiology, of which I was the representative. My first experience with the candidate was in connection with his petition to the Graduate School to be exempted from the foreign language requirements for the Ph.D., which had never been waived before that time, and I remember vividly the consternation this request raised in the Graduate School community. Ingle's examining committee took account of the sixty high-quality scientific papers that he had already published and concluded that Ingle had demonstrated his fitness for a doctorate. There was no dissent among the committee members.

The Ingle case was a landmark decision for the Graduate School at Minnesota and was followed by many more examples of breaking traditional rules and regulations at that institution. I was somewhat surprised, therefore, that Ingle himself made no mention in his autobiography of his stubborn refusal to bother with things like foreign language requirements, which he undoubtedly considered much less important than learning how to remove part or all of a rat's pituitary gland at the age of weaning. He was, of course, right, but in his mention of his Ph.D. examination he refers only to the fact that he was asked only one question relating to psychology, his major field, the examination being dominated by questions on biology and physiology.

After completing his graduate studies at the University of Minnesota Ingle moved to the Mayo Clinic, where he

was a Mayo Fellow for four years and collaborated with E. C. Kendall's group in studies of the hormones of the adrenal cortex. He then became a Cox Medical Research Fellow at the University of Pennsylvania, where he worked for three years under the sponsorship of Dr. F. D. W. Lukens.

After the termination of the Cox Fellowship, Ingle worked for the Upjohn Company in Kalamazoo, Michigan. In his twelve years there he became a senior research scientist and conducted a basic research program in endocrinology without pressure to work on problems of specific importance to the company. Yet he became restive, and when he was offered a professorship of physiology in The University of Chicago's Ben May Institute, he left Michigan for Chicago, remaining there from 1953 until his retirement twenty years later. Chairman of the Department of Physiology for nine years, he was not happy as an academic administrator and relinquished the post before he retired.

INGLE AND THE NEW FIELD OF ENDOCRINOLOGY

As noted above, Ingle came onto the scientific scene when endocrinology was emerging as a major field of science. He offered the new field freshness of approach and imagination, strict critical thinking, and boundless energy for painstaking work. Perhaps his greatest asset was his ability to define problems in a way that could be answered by direct observation in experimental situations. In reviewing his very large scientific output, it is obvious that he excelled at asking specific questions and spared no pains in devising methods to answer them.

Ingle is responsible for at least three signal advances in endocrine science—development of a bioassay for adrenal cortical hormones that facilitated the purification of cortisone, documentation that the adrenal cortex and the pituitary gland interact by a negative feedback mechanism, and

characterization of the permissive role of adrenal hormones in homeostatic control mechanisms. His contributions are described in detail in his own autobiography¹ and in E. C. Kendall's autobiography.²

The first of these advances stemmed from a 1934 paper in which Ingle (together with W. T. Heron and W. M. Hales) reported that repetitive contraction of skeletal muscle requires an intact adrenal cortex. Ingle suggested to E. C. Kendall that this phenomenon could be utilized as a bioassay for the activity of adrenal cortical extracts. Kendall immediately realized the potential of such a bioassay in the purification of adrenal hormones and invited Ingle to join his group at the Mayo Clinic, an appointment that Kendall described as a turning point in the purification of the glucocorticoid hormone cortisone.² The assay provided reliable data as to which purified fractions contained the active principle and gave the Mayo group an advantage over competing laboratories that lacked such an assay. During these early studies he characterized the relation between the adrenal gland and salt and water metabolism, a phenomenon that subsequently became the basis of another bioassay system that led to the recognition that the adrenal cortex also secretes a mineralocorticoid hormone, later characterized as aldosterone.

Another side observation of the studies at the Mayo Clinic led to his second major contribution, namely in 1937 Ingle observed that the administration of adrenal cortical extracts or purified glucocorticoids to intact rats causes atrophy of the adrenal glands. Adrenal atrophy could be prevented by the simultaneous administration of pituitary extracts, and he subsequently established in collaborative work with Herbert M. Evans and Choh H. Li that the changes in adrenal size and activity are mediated by the pituitary hormone adrenocorticotropin. The elucidation of the feedback relation between the adrenal cortex and the pituitary

gland served as a paradigm for similar control mechanisms in other endocrine systems.

His third major contribution evolved from his studies of the physiological actions of adrenal steroid hormones, a train of thought that led to excursion into diverse aspects of physiology, including studies of the effects of adrenal steroids on carbohydrate physiology, investigations on the pathogenesis of hypotension (shock) in animals with adrenal insufficiency, and the effects of severe stress on animals. The damaging effects of stress were widely believed to be due to hypersecretion of the adrenal cortex. However, Ingle showed that the characteristic damaging effects of stress are produced when adrenal steroids are supplied to adrenalectomized animals at a constant but not excessive rate of administration. He thus deduced that the role of the adrenal cortex in the stressed state appears to be due to a subtle "permissive" or supporting role rather than as the primary mediator of the stress reaction. This paradigm has had an enormous impact on the analysis of endocrine systems.

PERSPECTIVES IN BIOLOGY AND MEDICINE AND
THE ETHICS OF RESEARCH

At Chicago Ingle founded a hybrid journal of a type that had never existed before. *Perspectives in Biology and Medicine* published papers from the interface between the biomedical sciences and the humanities. To Ingle *Perspectives* was the forum where the "ordinary fellow" could explore and integrate "two cultures"—a term he coined long before E. P. Snow applied it as a catch phrase for the gap between humanists and scientists. With the encouragement and help of The University of Chicago Press, Ingle provided a single publication medium to serve the two groups, demonstrating in a practical way that differing points of view could have a commonality of objectives.

Perspectives published various types of speculative essays on basic science and the ethics of biomedical research—particularly useful at a time when serious problems so often involve situations where biological science and ethics intersect. Having first provided a forum for the rational presentation of varying viewpoints, Ingle used the journal frequently to air his own analyses of such problems.

Ever careful to give credit to his own research staff, Ingle felt particularly strongly about the impropriety of senior research directors who report the results of students without acknowledging their ideas and implementation. At the Endocrine Society's annual banquet in 1959, his presidential address included an elaborate fable about a scientist born with "a mutation that enhanced the ability of the brain to function creatively." This mutation had come about when a clergyman grandfather was struck by a single neutron while "bent over an ice cream freezer at a church social." Skipping the son, who became a mail carrier, it manifested itself in the grandson.

Tongue in cheek, Ingle went on to describe how the grandson became a promising graduate student and made an entirely independent discovery that greatly pleased his advisor. The advisor asked the young man if he might disclose the finding publicly in an important address he was about to deliver. Receiving consent, he dutifully reported that his graduate student had made an exciting discovery. To no one's surprise but the student's, however, the next day's headlines read, "Professor X announces a major discovery." Professor X then became a noted participant in scientific seminars and a frequent guest lecturer on the subject of the student's discovery.

According to Ingle's fable, Professor X rode to fame and fortune while the young student, if not ignored, was recognized only by serious students of his field. Promoted rap-

idly in prestigious academic institutions, he soon became a full professor with productive graduate students of his own. One day, a student reported to him a highly significant result gained from entirely independent studies. As it happened, the young professor was just about to give a talk on the work going on in his department, and he asked the graduate student's permission to report his unpublished results. He felt a little qualm when he remembered his own dismay when credit for his work as a student went to his academic sponsor but reminded himself that he provided the intellectual climate in which his students worked and the stipends to live and develop into creative scientists. And so it was that the grandson announced his student's innovative study, and the next day the headlines read, "Professor Y announces spectacular new scientific results"—with predictably favorable consequences to his career.

This tale occupies eight pages of Ingle's autobiography, where he details several stages of the successful scientific career: appointments to journal editorships, membership on foundation and government grants committees, administrative posts. An inveterate storyteller but never abrasive, he used a gently satirical tone to criticize people of his own ilk. He poked fun at human frailties but was generous and forgiving.

AWARDS AND HONORS

Ingle received much honor and acclaim for his contributions to endocrinology. He was invited to lecture many times at home and abroad. He was awarded the Honorary Doctor of Science degree by the University of Idaho in 1962, received the Koch Award of the Endocrine Society, and was elected to the National Academy of Sciences in 1963. He was given the Outstanding Achievement Award of the University of Minnesota in 1964, the Roche-Organon

Laurentian Hormone Conference Award, and the Upjohn Prize. He was elected a fellow of the American Academy of Arts and Sciences and was given the Modern Medicine Achievement Award. He was a member of Phi Beta Kappa, Sigma Xi, Alpha Omega Alpha, the American Association for the Advancement of Science, the American Physiological Society, the Endocrine Society (president, 1959–60), and the Society for Experimental Biology and Medicine (president, 1965–67).

“My research efforts have been driven by curiosity,” he once wrote, when asked what motivated him to do scientific research. “The joy of the daily search has been enhanced by occasional discovery.”

He will long be remembered as a perceptive, careful, and creative scientist of broad intellectual interests—and as an unusually decent human being; definitely not, as he himself put it, “an ordinary fellow.”

NOTES

1. D. J. Ingle, *I Went to See the Elephant* (New York: Vantage Press, 1963).
2. E. C. Kendall, *Cortisone. Memoirs of a Hormone Hunter* (New York: Charles C. Scribner's Sons, 1971).

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