The Social Significance of Endocrinology

MORTIMER B. LIPSETT, M.D.

Presidential Address
62nd Annual Meeting of The Endocrine Society

It has become fashionable to decry the advances in technology for their lack of impact on the health of people and to belittle the achievements of the biomedical sciences. Chargaff is concerned about the “widespread revulsions from science ... and the distaste for experts on a narrowly defined set of matters that the rest of humanity really cares very little about.” Illich in his brilliant diatribe entitled “Medical Nemesis” carefully documents the major improvements in health that have resulted from good nutrition and sanitation, but he warns of “technical iatrogenesis” and, except for the limited area of infectious disease, denigrates the contributions of medical research to the improvement of the health status of large segments of the population. These are two rather typical laments from the litany of complaints about science in general, and about biomedical science and medicine in particular. And added to this general dissatisfaction is the often expressed concern for the relevance of research. But, as I shall show, endocrinology, renewing itself constantly from the well of basic biology and often without specific commitment to relevance, has been able to exert a large and measurable effect on the health of peoples.

Many have documented the high benefit/cost ratio of medical research, and tonight I shall stress those achievements of endocrinology that have improved the health and well-being of thousands or millions of people. I should therefore like to entitle this brief talk, “The Social Significance of Endocrinology.” But in so doing, I equally applaud those many tours de force of the laboratory and the clinic that are reported in our journals for they often give the initial insights that signal major advances.

In the first encyclopedia of endocrinology published in this country in 1922, Garrison noted “we are what we are, bodily, mentally, sexually, emotionally largely through the balance or imbalance of certain secretions discharged in minute quantities into the blood by a set of glands.” How right he was—and in all those aspects of life the hormones have been shown to be important.

In this same volume are summarized many observations and theories about an epidemic of endocrine origin that has been halted as a result of endocrine research and could be ended by its application. The epidemic was thyroid goiter and cretinism, and it involved millions of people. In the early 1900s, up to 3% of affected populations were cretins and several times that number had goiter. Then, almost 60 years ago, Kimball and Marine demonstrated the efficacy of iodine in the prevention of goiter, and soon after, its value for the prevention of cretinism was amply proved in Switzerland and elsewhere. In the report of their first clinical trial, Kimball and Marine stated “Not a single pupil in whom the thyroid was normal last year and who took iodine showed any enlargement, while of those not taking iodine, 20% showed definitely enlarged thyroids and some moderately enlarged goiters.” Their work is a superb example of preventive medicine at its best and, except for the vaccines for infectious disease, was probably the best medical measure introduced into preventive medicine since Lind’s discovery of the antiscorbutic effect of lime juice. Endemic goiter persists today in many underdeveloped countries and still remains a topic for investigation. In fact, as recently as 15 years ago a successful clinical trial of iodine prophylaxis against cretinism was carried out in the highlands of New Guinea. Thus endocrinology, as a result of basic research, paid its dues to preventive medicine many years ago, and continues to do so even today.

To pursue the theme of large scale benefits of endocrine research, one should look at the oldest of the fields, reproductive endocrinology. The relation between the testis and virility was appreciated more than 3000 years ago, for it is written in Deuteronomy that the man without stones shall not enter the temple—the ancients equated the loss of the testes with the loss of virility. Aristotle described the effects of castration in the bird and likened the changes to those of castration in the boy. Berthold, in the middle of the last century, studied the effects of androgen deprivation on target tissue and showed that androgens were an internal secretion of the testis. Almost 100 years later, testosterone was isolated, analyzed, and synthesized, providing the firm bases for male reproductive endocrinology.

When Aristotle was carrying out research on the effects
of castration over two thousand years ago, the possible risks entailed in the pursuit of new scientific knowledge were not a desideratum of research, and castration was subsequently used for what we now characterize as immoral purposes—the production of eunuchs in the ancient world and the even more recent use of castrati in the choirs in Rome. Nevertheless, this base of knowledge and its further scientific amplification permitted one of our endocrinologists and a Nobelist, Charles Huggins, to show that castration was useful in the treatment of prostatic cancer. Today, surgical and medical castration are the primary therapies for this second commonest cancer of men, and Dr. Huggins’ research on the action of the male hormone initiated the modern era of endocrine treatment of cancer.

Female reproductive endocrinology is responsible for a continuing and evolving sociologic revolution. Its scientific history takes form with the identification of the ovarian follicle by DeGraaf in 1692 and the correct surmise of Prenant in 1898 that the corpus luteum was a gland of internal secretion. Ludwig Fraenkel in 1903 proved the hypothesis communicated to him by his dying teacher, that the corpus luteum was concerned with the protection of the embryo. The subsequent studies of Leo Loeb, Allen, Doisy, and Butenandt led to a reasonable framework of the chemistry and physiology of the female sex steroids and their roles in reproduction.

During the ensuing years, many endocrinologists explored the ovary, its regulation on the one hand and its control of the uterus and implantation on the other. The discovery by Pincus and his coworkers that a combination of estrogen and progesterin would inhibit ovulation was a direct result of their studies of these compounds in infertility. It is hard to appreciate the magnitude of the response to this discovery. At this time, it is estimated that about ten million women in this country and sixty million women around the world are using oral contraceptives. The changes in social mores, deplored by some and welcomed by others, have added new dimensions to our way of life, and the ability to regulate family size is changing the fabric of our society.

It is difficult to categorize the oral contraceptives. If we call them agents of preventive medicine, we may be accused of immorality. And they are certainly not therapeutic. I would say rather that they testify to vigorous biomedical research responding to a human need with one of the most effective pharmaceutical agents that has ever been made available. This saga of endocrine research, progressing from the observations of the clinician, to the detailed research of the biologist and chemist, and then back to the clinic, illustrates the great potential of the interactions among laboratory science, clinical investigation, and medical practice to the ultimate benefit of mankind.

But we have been made bitterly aware of the side-effects of oral contraceptives and have been accused of taking chances with the health of women by those who have been unwilling to assess comparative risks and benefits. Fortunately, the risks are being accurately defined and, more importantly, continuing research in endocrinology is leading to a new and almost surely less risky contraceptive technology.

This line of investigation had its origin in the studies of Geoffrey Harris, who 40 years ago initiated explorations into the role of the hypothalamus in the regulation of pituitary function. And the field came to fruition with the identification of hypothalamic releasing hormones during this last decade. Three years ago, two members of this Society, Andrew Schally and Roger Guillemin, shared a Nobel prize, in part for their identification of the releasing hormone synthesized in the hypothalamus that regulated the secretion of the gonadotropins and, in so doing, determined the ovulatory menstrual cycle. And others of us, one of whom is your past President, Ernst Knobil, have shown that this gonadotropin-releasing hormone must be secreted periodically in order for the normal pattern of gonadotropin secretion and ovulation to ensue. This has led to clinical trials of long-acting analogs of gonadotropin-releasing hormone which, by substituting continuous for periodic action, prevent ovulation. The trials have been most promising and one would predict few side-effects.

Several years ago during a visit to China, I became aware of another important use for gonadotropin-releasing hormone that has affected the lives of thousands of people. An important source of protein in parts of China is carp, raised in fresh water ponds and in the rice fields, but carp do not spermiate under these conditions, and the use of gonadotropins proved to be too expensive. However, analogs of gonadotropin-releasing hormone were tested and found to be effective, cheap, and easily administered by the farmers. So here we have been able to move from human endocrinology to a technique for increasing fish production and, thereby, human protein consumption.

I shall not dwell overly long on diabetes mellitus, although the years of human life that have been saved since the discovery of insulin in 1921 must number in the hundreds of millions in this country alone. The dogged pursuit of methods for eliminating the complications of diabetes mellitus has already yielded further years of useful life, and current research seems to place us on the road to achieving near normal regulation of the blood sugar. Since there are about a million patients with insulin-dependent diabetes mellitus in the United States alone, the total effort of endocrinology is and will be significant for public health. And we cannot overlook the salvage of thousands of infants every year born to mothers with frank diabetes.

I have mentioned how research in male reproductive
endocrinology led to palliative treatments for prostatic cancer. But we know how even more basic research into the mechanism of hormone action has given the physician the opportunity to prescribe rational therapy for the woman with breast cancer. Your incoming President, Elwood Jensen, in his studies of estrogen action, described the estrogen receptor 20 years ago, and the influence of this discovery on studies of all steroid hormones has been revolutionary. Additionally, the presence of estrogen receptor in breast cancer was shown by Jensen and others to predict responsiveness to endocrine therapy in women with this disease, and a year ago an international consensus was reached on the recommendation that all women undergoing mastectomy have estrogen receptor measurements performed. This achievement, taking a fundamental discovery about a biologic process to the point where it has clinical application to the most prevalent cancer in women, has just been recognized by the General Motors Award in Cancer Research to Dr. Jensen. It would have been hard to predict that an apparently clinically irrelevant finding would have such wide clinical applicability.

Techniques have often been accorded cursory recognition because they have been thought to be derivative. But new techniques of measurement have proved indispensable in every area of human endeavor because they have led to that quantum jump of discovery that a field is privileged to experience on rare occasions. One could cite the invention of the chronometer to measure longitude for its revolutionizing effect on international trade, the development of double entry bookkeeping as a necessary component of modern commerce, and the radioimmunoassay for its contribution to endocrinology, medicine, and many other areas of the life sciences. Our past President, Rosalyn Yalow, and Sol Berson conceived, developed, and exploited the radioimmunoassay technique that has been used by you in more than 75% of the papers presented at this meeting, and the Nobel prize to her in 1977 recognized the incalculable benefits of the radioimmunoassay technique. It has permitted the diagnosis of endocrine diseases that were previously unknown, made possible the detection of hypothyroidism at birth, facilitated the search for viruses, the identification of pathogen, and the measurement of drugs, and new applications appear every day. Surely this is a sufficient answer to Illich’s “technical iatrogenesis.” This discovery of a measurement technique developed from exploration of physiologic processes in man and proved again Pasteur’s thesis that chance favors the prepared mind. It proved, as well, that support of research, unfettered and nondirected, is often repaid to the public in value many times the original investment.

There are other areas where endocrinology has been important on the world health scene. The isolation of cortisol was not goal-directed, but it and its congeners are now potent therapeutic agents in many diseases. Infertility, a common problem for thousands of couples, yields with increasing frequency to endocrine therapy. And I could continue but I hope that I have reinforced your belief that endocrinology is an essential discipline for world health.

But one wonders with this cataloging of achievement whether we as endocrinologists have reached the end of our major contributions to people of this country and of the world? I would predict not. And the few possibilities that I can envision may be easily surpassed as a result of fundamental discoveries yet to be made.

In veterinary endocrinology, researchers are studying and using hormones to increase the rate of gain of livestock. Our ability to synchronize estrous cycles in livestock permits economical use of artificial insemination. The analysis of hormonal regulation of pregnancy in many species has facilitated embryo transfer, a technique that is becoming increasingly valuable for improvement of species and commercial breeding.

And in the human, what lies ahead? Does our increasing knowledge of endocrinology of the central nervous system pose significant dangers? Does our burgeoning information about peptidergic neurons, the distribution of these peptides, and possible regulation of synthesis, imply that we, as endocrinologists, will be able to supply physicians or politicians with mood-altering agents? We do need to look at our research and examine its probable paths of application, much as have the scientists concerned with recombinant DNA techniques. But as we do this, we must remember that the possible benefits of endocrine research in the central nervous system are great. For example, we stand on the threshold of the practical application of endocrinology to problems of pain, and somewhat more speculatively, one might predict that some mental diseases will yield to endocrine research.

Although endocrinology is now firmly entwined with oncology, the great advances in the merging of these fields lie ahead of us. The new classes of growth substances that exert profound effects on cell growth, differentiation, and division are increasingly being defined by endocrinologists and cell biologists. These growth substances, already shown to be of biologic significance in experimental tumors, will surely change our ways of thinking about and treating human cancer.

I have spoken of androgen deprivation as a treatment for cancer of the prostate. But a more common cause of disability in older men is benign prostatic hypertrophy, a disease of high prevalence and morbidity. Endocrinologists are now defining those factors that maintain or stimulate prostatic growth. I will prophesy that we shall learn how to manipulate the steroid hormone-receptor interaction selectively so that hormonal stimulus can be denied to one tissue while maintaining it elsewhere, and...
in so doing, take an important step in preventing or reversing benign prostatic hypertrophy.

Osteoporosis is a leading cause of disability in our aging population. In this area one can make a confident prediction that ongoing and future endocrine research will largely ameliorate and possibly solve this problem.

And finally, we should recognize that we are now in the midst of a biologic revolution—the merging of much of pharmacology and endocrinology. This interaction has made possible the treatment of such disease conditions as infertility, some tumors, cancer, some types of hypertension, and other diseases.

Some of us in the past have felt that it was difficult to popularize endocrinology because it was not identified with a disease. I submit that since endocrinology is one of the great integrating systems of the body, we can claim with considerable justification that our research takes us into every area of health and disease. But we have not seen ourselves as agents of change in preventive medicine, nor has our own image been that of a profession or a specialty that exerts a large influence on the health of people, and, yet, we have. We have come out of the time when, as Fuller Albright said, “Every rare disease was supposed to have endocrine cause” to an era in which a physician, given the tools recently placed at his disposal, can succor the individual with rare and unusual disease and participate in large public health ventures with equal facility.

Endocrinology has a noble past, an exciting present, and a challenging future. I have spoken of some of these. As Shakespeare said, “There is a history in all men’s lives, figuring the nature of the times deceased, the which observed a many may prophesy, with a near aim, the main chance of things as not yet come to life, which in their seeds and weak beginnings lie intreasured.” We have in endocrinology, many seeds and weak beginnings, which, in their flowering, will sustain and improve human life.