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GEORGE WASHINGTON CORNER

12 December 1889 — 28 September 1981

Elected For.Mem.R.S. 1955

By Lord Zuckerman, O.M., F.R.S.

George Washington Corner III died at the age of 91 on 28 September 1981. For many years he was both the dominant and the most respected figure in the anatomical world of America. He was also an inspiration to anatomists the world over in a period when the subject, because of its tardiness in responding to the challenge of the experimental method, had all but become the Cinderella of the medical sciences. Corner was a man of wide and scholarly interests, a distinguished pioneer in the experimental study of the endocrine control of the reproductive cycle, and a notable medical historian.

He was born in Baltimore on 12 December 1889, the eldest of the three children of George Washington Corner II, a well-to-do merchant. His mother, Florence Evans, was, like her husband, a descendant of New England British stock. The Corners had been long established in Baltimore, to which George's great-grandfather, James Coleman Corner, had moved from another part of Maryland at the end of the eighteenth century, and where he had founded a flourishing shipping firm. George's maternal grandfather, Henry Evans, had been brought as a boy to America from Somerset in England. He was one of the pioneers of the food-packing industry. George had a happy childhood. Both his parents were strict Methodists, and he accepted without demur the discipline of daily family prayers. After 6 years in one of the city's public schools, he moved at the age of 14 into the Baltimore Boys' Latin School, an establishment that catered for the sons of well-off middle-class families. Latin, English and Mathematics dominated the curriculum, but George was able to satisfy a natural bent for science through voracious reading and by experimenting at home with simple electrical apparatus.

He entered Johns Hopkins University in 1906. The University was then 30 years old, and numbered about 750 students, only some 150 of whom were undergraduates, the remaining 600 being either medical students or in postgraduate work. Its staff already included several
outstanding men. In his second year, Corner dropped Latin to read general biology and comparative anatomy, two subjects in which he shone. He took his first degree in 1909, after which he spent some months in the U.S. Bureau of Fisheries Laboratory in North Carolina, an institution that was designed on the model of the Plymouth and Naples marine laboratories. There, in the company of a number of visiting senior scientists, he embarked on his first piece of research, the life-cycle of the protozoan *Cothurnia*. A record of his findings was published in 1911 (1) in the *Johns Hopkins University Circulars*.

On returning to Baltimore, Corner had to decide whether to work for a Ph.D. degree in zoology or to proceed straight to medical school. He chose the latter course, and in October of 1909 entered the Johns Hopkins Medical School, which was then under the direction of the famous Dr William H. Welch. At the time, Johns Hopkins was the only school in the United States in which all the medical disciplines were represented. Some of the departments were directed by men who were to make medical history, among them John Abel, the chemist who isolated and determined the chemical structure of adrenalin, and George Whipple, who in 1934 shared the Nobel Prize for his contribution to the discovery of the treatment of pernicious anaemia with liver extract. Harvey Cushing, the 'father' of modern brain surgery, was also still there. The school had a vigorous medical history club and library containing a valuable collection of medical classics.

Corner qualified in 1913 after the statutory four years of medical studies, during which he spent a summer vacation attending lectures in Freiburg, including a course delivered by the world-renowned Ludwig Aschoff. He spent another vacation working in a Grenfell Medical Mission in Labrador, to which he returned for a few months after graduating. There it was that he first met Betsy Copping, whom he was later to marry. She was the daughter of a New Hampshire Congregational minister, and had volunteered for work as a school teacher at the Mission Station at Battle Harbor.

The research programme of the Johns Hopkins Anatomy Department, which Corner joined as an 'assistant' in 1913, determined his own enduring scientific interests. Franklin Mall, the head of the Department, was then the most distinguished morphological embryologist in the world. Florence Sabin, whose fame as a teacher became all but legendary, was well known for her work on the origin of blood cells. She also taught microanatomy and neurology. There was also Herbert M. Evans, one of the pioneers of the study of the functions of the pituitary gland. As a student Corner had selected as a research project the duct system of the pancreas, the results of his enquiries being published in the *American Journal of Anatomy* (2) the year after he qualified. As an assistant in Mall's Department he felt constrained to follow his professor's suggestion that he turn his attention to the development of the corpus luteum.
of the mammalian ovary. The fruits of his first piece of work in this field were published in 1915 (3) under the title ‘The corpus luteum of pregnancy as it is in swine’.

After a year as ‘assistant’ in the Anatomy Department, Corner did his statutory year’s internship in the Department of Gynecology. He then left Baltimore, having accepted an invitation from Herbert Evans to become an assistant professor in the Department of Anatomy in Berkeley, California, to the directorship of which Evans had just been appointed. Corner remained with Evans from 1915 until 1919, marrying Betsy Copping a few months after he had moved to California. In those days one could set up home on a salary of $125 a month.

Once again, Corner found himself in an inspiring, even if smaller, company. Evans was a man of powerful and tireless intellect, and was destined to build a Department whose work would have a lasting impact on the development of the whole subject of endocrinology. Another new colleague was Philip E. Smith, whose name, too, was to put a stamp on the blossoming subject of endocrinology. In this company Corner continued with his own researches into the reproductive cycle of the pig. His interest in the history of medicine never waned and, in addition to his load of conventional anatomical teaching, he continued to give, as he had at Johns Hopkins, a course of lectures on the history of the subject.

In 1919, at the age of 30, Corner returned to Johns Hopkins as Associate Professor of Anatomy under Lewis H. Weed, who had by then succeeded Franklin Mall as head of the Department. As always, Corner was moving from one exciting environment of research to another. Close to the Medical School was the Carnegie Institution’s powerful Department of Embryology, directed by George Streeter, on whose staff was Oscar Riddle, who was then working on the reproductive physiology of pigeons. In the Phipps Psychiatric Clinic of Johns Hopkins was a brilliant young experimentalist, Curt Richter, whose observations on the rhythmic cycles of activity in albino rats Corner was soon to relate to Evans’s and Joseph Long’s discoveries about the oestrous cycle of an animal that had not yet become the familiar experimental animal it is today. He himself arranged to continue his enquiries into the life of the corpora lutea of the pig, which in Berkeley he had only been able to follow until about a week after ovulation. He also started a series of researches into the causation of menstruation, working on the rhesus monkey. During the period that he was a member of Weed’s Department, Corner attracted to his own laboratory several young research workers, some of whom, among them Franklin Snyder and Alan Guttmacher, were also to make their names in the story of reproductive physiology.

In 1923, now 34 years old, Corner was chosen as the Director of the Anatomy Department in a new medical school about to be built in Rochester, New York, with the help of a considerable endowment from the Rockefeller Foundation and from Mr George Eastman, President of
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the Kodak Company. Since it was to be a totally new medical school and teaching hospital, Corner was asked to direct the design of the Anatomy Department, and was encouraged to go abroad for the year during which building operations were to take place. Accordingly, he spent the period from September 1923 to June 1924 in the Physiology Department of University College London, which at the time was directed by Ernest Starling and William Bayliss (the latter had been succeeded by A. V. Hill by the time Corner arrived). Corner took advantage of his stay to consult many of the leading figures in British medical science about the plans for the new Rochester school, and also to recruit some of the staff that was wanted. He saw a great deal of Grafton Elliot Smith, then Professor of Anatomy in University College, and of H. H. Woollard who was to succeed to Elliot Smith's Chair. He also attended lectures given by Dr Charles Singer, the most distinguished medical historian in the United Kingdom. The two became close friends.

After leaving England in June 1924, Corner spent two months in the University of Strasbourg before returning to the United States. In Strasbourg he became acquainted with three men—Paul Bouin, Paul Ancel and Robert Courrier—who were playing a central part in the development of French research in the field of reproductive physiology. Like Corner, Courrier was to become a Foreign Member of the Royal Society (at 87 he is still the Secrétaire Perpetuel of the Académie des Sciences).

For 16 years, from 1924 until 1940, Corner directed the Anatomy Department in Rochester, and it was here that he carried out most of his best known scientific research. Organizing a new department was no easy task, but fortunately he had been able to recruit to his staff some outstanding men, among them the experimental embryologist, R. K. Burns. He was also able to find in Willard Allen, a young biochemist in the new school, a collaborator with whose help Corner was to isolate progesterone, the hormone of the corpus luteum. Busy as he was, he also continued with his studies of medical history.

In 1940 Corner resigned his Chair in Rochester and returned to Baltimore to succeed Streeter as Director of the Carnegie Institution of Washington’s Department of Embryology. Because this Department was physically part of Johns Hopkins University, the move meant that Corner was returning to the company of old friends and colleagues. Robert Burns accompanied him from Rochester, and he was also able to recruit to his staff Dr Sam Reynolds, then a leading authority on the physiology of the uterus. During Mall’s and Streeter’s reigns, the emphasis of the Department’s work had been on descriptive morphological embryology. Under Corner’s, which lasted 15 years, it shifted significantly to experimental embryology.

Two years before his Carnegie Directorship was to end, Corner was given leave to spend a year as Eastman Visiting Professor at Oxford, an
appointment that carries with it a Fellowship at Balliol. He was also given ‘house-room’ in the Department of Anatomy, then presided over by Sir Wilfrid Le Gros Clark. On his return to Baltimore, Corner devoted his final year as Director of the Department of Embryology to winding up his affairs as an active laboratory scientist. He also had to decide what to do next because, although he had reached the retirement age of 65, he was not only still full of vigour, but anxious for gainful employment, since he had saved little in the 40 years he had already spent in academic work. Once again Dame Fortune stepped in. The Trustees of the Rockefeller Institute, of which the physiologist Dr Detlev Bronk had just become the Director (while still acting as President of Johns Hopkins), had decided that a history should be written of the Institute’s first 50 years. Corner accepted an invitation to undertake the task, and in 1955 moved with his wife to New York, for what was assumed at the start would be a period of only two years. The job took five years. His book (97) was delivered to the Trustees in 1960, and appeared in print in 1964.

In 1960, and now 71 years of age, Corner was invited to become the Executive Officer of the American Philosophical Society in Philadelphia, the oldest and in many ways the most prestigious of the learned societies of the United States. He held this office for 16 years before, at the age of 88, he handed over his executive duties to Mr Whitfield J. Bell Jr, while retaining office as editor of the Society’s publications, and chairman of its Committee on Research. He relinquished the latter responsibilities only in 1980. Those who attended the joint meeting of the American Philosophical Society and the Royal Society that took place that year in London will remember Corner as a man whose appearance totally belied his age. He continued working until the end, and in his 92nd year, a few days before his death, he sent the Philosophical Society’s Research Committee handwritten assessments of some grant applications that had been referred to him.

**Scientific achievements:**

**THE PHYSIOLOGY OF REPRODUCTION**

To appreciate Corner’s considerable contribution to our understanding of reproductive mechanisms, it is necessary to bear in mind how little was known about the nature of the phases of the mammalian sexual cycle when he embarked on his first studies. For example, although the duration of the menstrual cycle was known, the time when ovulation occurs in the cycle was still a matter of speculation when Franklin Mall suggested in 1913 that Corner investigate the development of the corpus luteum. What Mall was hoping was that an understanding of the formation of the corpus luteum might provide a means of determining the age of early human embryos. A corresponding ignorance prevailed about the ‘lower’ mammals. That ovulation is in some way associated
with the phenomenon of ‘heat’ (oestrus) was obvious, but that was all. No
one knew how long the oestrous cycle lasted in the rat or the pig or, for
that matter, in any other mammal. The fact that the cycle is under the
control of steroidal hormones, which themselves are controlled by
secretions of the anterior lobe of the pituitary, was not to be revealed for
many years to come.

The corpus luteum of the pig

Corner began his studies by collecting and sectioning for microscopic
study the ovaries of pregnant pigs. On the basis of cytological differences
in the luteal cells, he posited seven stages in the 115–120 days of
pregnancy, and showed that the corpora lutea that develop from the
ruptured ovarian follicles degenerate by the fifteenth day. The results of
this piece of research were published in 1915 (3), but in Corner’s own
judgement they added little to knowledge of the sow’s reproductive cycle.
What followed certainly did, for in Berkeley he was able to collect the
ovaries of sows that had been under observation for signs of oestrus
before they were slaughtered. In this way Corner discovered that
ovulation takes place on the first or second day of oestrus, and that it
occurs spontaneously, and not as a result of the act of mating, as in the
rabbit. He was also able to settle once and for all the disputed question
of the cellular origins of the corpus luteum by showing that not only the
granulosa cells of the follicle, but also the cells of the theca interna, by
which the former are surrounded, become transformed into luteal cells.
Several years later Corner demonstrated that the same process of
development applies to the human corpus luteum and to that of the
rhesus monkey.

During the time he was carrying out these studies, major advances in
our basic understanding of reproductive processes were being made by
other research workers. In 1917, Stockard and Papanicolaou of Cornell
Medical School had discovered that ovulation in the guinea-pig is
associated with specific changes in the vaginal epithelium. Herbert Evans
and Joseph Long made use of this fact to develop the ‘vaginal smear
technique’, with the help of which they showed that oestrus and ovulation
recur approximately every five days in the unmated albino rat (Long &
Evans 1922). Once this had been established, it was possible to correlate
the cyclical changes that occur in the ovaries with those undergone by the
uterus and other accessory reproductive organs. While this work was
going on, Philip Smith was perfecting, in the same department, the
surgical technique of hypophysectomy in the rat, and opening the way to
an understanding of the control of the hormonal secretions of the ovary
by those of the pars distalis of the pituitary gland.

With all this new knowledge as background, Corner was able to
complete his analysis of the changes that take place in the ovaries and
accessory reproductive organs of the sow. The results were published in
1921 (14) in a monograph that soon became a model for corresponding studies of other mammals. In his autobiography Corner provides a summary of his findings in language so simple that it completely disguises the arduous and meticulous work from which his conclusions were drawn.

'...immature follicles up to five millimeters (1/2 inch) in diameter are always present in mature sows. At intervals of about twenty-one days, several follicles suddenly enlarge to a diameter of eight to ten millimeters. On the second day of estrus, they rupture and discharge their ova into the oviducts. On the fourth day after ovulation the ova reach the uterus, where if they are not fertilized by mating with a boar, they degenerate and disappear. I could find no ova later than six days after ovulation. Meanwhile the discharged follicles are converted into corpora lutea which, reaching full development about ten days after ovulation, put forth progesterone to condition the endometrium (uterus) to receive and nourish the embryos.

'The preparation for pregnancy is characterized by a great increase in complexity of the endometrial glands. I have called this changed state 'progestational proliferation'. As seen in women, gynecologists have named it the premenstrual stage. If the ova are not fertilized, the corpora lutea degenerate, beginning on about the fifteenth day. The endometrium, no longer supported by progesterone, reverts to its original state, and another estrous period soon sets in. If the ova are fertilized, however, the corpora lutea persist, maintaining the progestational state of the uterus until the end of the pregnancy.'

Corner was neither the first to describe the nature of 'progestational proliferation' nor to attribute it to the influence of the corpus luteum. Born, of Breslau, had predicted a hormonal influence of the corpus luteum at the turn of the century, and Paul Bouin and Paul Ancel of Strasbourg had given substance to the idea as early as 1910 (Ancel & Bouin 1910). What Corner's monograph did was to provide what he called 'a basic scheme' with which to compare what went on in the oestrous cycle of the sow with the cyclical changes that characterize other mammals. He was in no sense immodest in later describing the publication of his monograph as marking his emergence as 'an authoritative scientific investigator'. Nor, in the light of his increasing understanding of the nature of the oestrous cycle, was it surprising that he had immediately realized the significance of the periodic changes that characterized the running activity of the albino rats that his new colleague at Johns Hopkins, Curt Richter, had found so puzzling. Richter had already made his mark in studies of natural food preferences in the rat, and had turned his attention to the amount of time the animals exercise each day on wheels linked to their cages. He had noted that the females, but not the males, were most active every fourth or fifth day, and had wondered
whether this had anything to do with a sexual cycle. But he was unable to
find published and reliable information about sexual periodicity in the
rat. Soon after Corner’s return to Baltimore, he called on him to discuss
the matter. Corner immediately linked Richter’s findings to Evans’s and
Long’s as yet unpublished observations, which showed that the unmated
female albino rat comes into heat about every fifth day. Later, when
describing the occasion, Corner wrote:

‘There is no thrill quite like that which a scientist feels when two
previously unrelated facts suddenly snap together to teach him
something new. We [Corner and Richter] fairly chattered with
excitement as I examined other rats, some in high activity, some low,
and I showed Richter that I could tell one from the other by looking
at the vaginal spreads as well as he could by reading the cyclometers.’
(104)

The hormone of the corpus luteum

In his effort to isolate the hormone that the corpus luteum secretes,
Corner followed the classical procedures for unravelling any hormonal
process. He began by confirming what Fraenkel, Bouin and Ancel had
already demonstrated, namely that the removal of the corpora lutea from
the ovaries of mated doe rabbits prevents the progestational changes that
would otherwise occur in the endometrium, and that, as a consequence,
the embryos die. His next step was to show that if the ovaries of a doe
rabbit are removed 18 hours after she has been mated with a fertile male,
progestational changes still occur if the doe is injected daily for five days
with a ‘mush’ of corpora lutea. This having been established, the
biochemical work followed, carried out in collaboration with Willard
Allen. After several months of experimenting, crude but usable luteal
extracts were obtained by passing the vapour of boiling alcohol through
the minced corpora lutea of sows in an extraction column. Stimulation of
progestational changes in the uterus of young unmated rabbits, or the
maintenance of pregnancy in mated mature rabbits whose ovaries had
been removed, provided the necessary test for potency of the extracts.
Corner relates that on one occasion when he was about to carry out such a
test with a syringe full of extract, he stumbled on the steps of his animal
house, and ‘lost the world’s entire current supply of the hormone of the
corpus luteum’, which Corner and Allen had by then christened
‘progestin’.

The results of these experiments were published between 1928 and
1930 (24, 26, 27, 28), the period in which biochemists and chemists in
Germany, England and America had succeeded in demonstrating the
steroidal structure of the ovarian oestrogenic hormones. In 1923, Edgar
Allen, working with Edward Doisy (Allen & Doisy 1923), had isolated from whole ovaries a potent oestrogenic extract. Willard Allen then set about the purification of the extract that he and Corner had obtained, and in due course isolated crystals that were potent physiologically, and whose structure was established in collaboration with Oskar Wintersteiner of Columbia as being as shown below.

\[
\begin{align*}
\text{CH}_3 \\
\text{H}_3\text{C} \\
\text{H}_3\text{C} \\
\text{C}=\text{O} \\
\text{O}
\end{align*}
\]

By this time the Rochester workers were no longer on their own. As Willard Allen recorded in his ‘Recollections of my life with progesterone’ (Allen 1974).

‘Corner and I realized, of course, that there would be competition in the race for the isolation of the hormone. At least four groups in addition to ourselves, entered the race—Slotta in Breslau, Butenandt and Westphal in Danzig, Hartmann and Wettstein in Switzerland, and Hisaw and Fevold in Madison, Wisc. The crystalline hormone was announced in the summer of 1934 almost simultaneously by Winterstein and Allen, Slotta, et al., and by Hartmann and Wettstein. In a few months Butenandt and Schmidt had converted pregnanediol to progesterone and Fernholz had synthesized the hormone from stigmasterol. These endeavors established the structural formula in record time. What had started as progestin in Corner’s laboratory in 1929 had now become an “international hormone” and by December 1934, an “international incident” was brewing. Wintersteiner received a letter from Slotta indicating that he (Slotta) and Butenandt had agreed that they would use luteo-sterone as a name for the hormone. This development did not appeal to us, as we had named the hormone progestin in 1930. On January 14, 1935 Corner dispatched a masterful letter to Slotta in which we suggested progesterone as a suitable name for the hormone. By giving up our name progestin, we hoped that Slotta would give up his luteo-sterone.’

In 1935 an international conference agreed that the new hormone should be called progesterone, and fixed the international standard as the specific activity of one milligram of the international standard crystalline preparation.
The menstrual cycle

As soon as he had become clear about the coordination of the changes in the reproductive organs that mark the phases of the sexual cycle in the sow, Corner set about the scientific analysis of the menstrual cycle. When, in 1921, he started this work, it was not clear what the endometrial breakdown that manifests itself as menstruation represents in relation to the phases of the cycle in the bitch or the sow. Some saw it as the equivalent of the phase of endometrial degeneration associated in some species with ovulation and oestrus. Others speculated that ovulation takes place in the middle of the cycle, and that menstruation is the external sign of the breakdown of the progestational endometrium that marks the degeneration of the corpus luteum when fertilization does not occur. It was towards the latter view, expounded by several experienced and scientific European gynaecologists, that Corner leant.

In 1923, after two years of study in which 11 rhesus macaques were killed at different times of the menstrual cycle (which Corner found had ‘a modal length’ of about 27 days), he reported (21) that ovulation had not occurred in some of his monkeys that had nevertheless menstruated. This observation confirmed what both Walter Heape and Margaret Van Herwerden had concluded (Heape 1896; Van Herwerden 1906) about the turn of the century from their post-mortem studies of monkeys, and at the same time controverted Robert Meyer’s gynaecological dictum, ‘ohne Ovulation keine Menstruation’. Later Corner attributed the unexpectedly high incidence of cases of ‘menstruation without ovulation’ to the fact that his animals were not fully mature.

He also noted (21) that when ovulation did occur, it took place about 12–14 days before the expected onset of menstruation. The endometrium was of the ‘interval’ or non-progestational type in two monkeys that had retrogressing corpora lutea in their ovaries, one of which was killed 9 days, and the other 18 days, after the onset of menstruation. The endometrium had the same structure in another monkey, whose ovaries contained a very early corpus luteum; it had been killed 12 days before the expected onset of bleeding. The endometrium of a monkey that was killed 10 days before the expected onset of menstruation was in an early phase of the ‘premenstrual’ or progestational stage; its ovaries contained an almost completely organized corpus luteum. That of a monkey in which a solid corpus luteum was found, and which was killed 7 days before the expected onset of bleeding, was distinctly ‘premenstrual’: i.e. ‘the surface epithelium is high, the glands are distinctly spiral in form, there are marked secondary projections into the glands, the glandular epithelial cells are high and their surfaces frayed, and the basal glands are increased so much that the endometrium appears on section to be of spongy texture’. Corner noted that the endometrium of the animal killed 12 days before the expected onset of menstruation and just after ovulation
had occurred—the ovum was found in the Fallopian tube—showed none of the 'characteristic changes which mark oestrus' in the pig, rat, mouse or guinea-pig; that is to say, there were no signs of endometrial degeneration such as vacuolar degeneration of the epithelial cells or an accumulation of leucocytes under the epithelium.

In 1927 Corner explained the significance of his findings (22) by relating them to the theory of the human cycle as it would have been based on the gynaecological observations of Fraenkel, Hitschmann and Adler, Magnus, Meyer and Schroeder. He wrote:

'Ovulation is a periodic function occurring regularly at about the middle of the interval between two menstrual hemorrhages. It is followed by the development of a corpus luteum at the site of the discharged follicle; and this structure, acting as a gland of internal secretion, causes changes in the endometrium (the well-known “premenstrual” changes first described by Hitschmann and Adler) by which it is prepared for implantation of the embryo. If the ovum is fertilized the “premenstrual” endometrium thus becomes the endometrium of early pregnancy. If, however, the ovum is not fertilized, the corpus luteum retrogresses, and at about the same time the “premenstrual” endometrium suddenly breaks down with resultant hemorrhage. Menstruation is on this theory merely a violent demolition of the “premenstrual” uterine edifice, some days after the expected tenant (the embryo) fails to arrive. Each menstrual period is therefore necessarily dependent on the occurrence of ovulation about two weeks before.'

It was this last belief—'ohne Ovulation keine Menstruation'—that Corner's own observations controverted. As part of the additional evidence, which he published in 1927 (22), he noted that one of his animals had been menstruating from a typical 'premenstrual' endometrium; laparotomy had shown that she had ovulated about fourteen days before. On the other hand another monkey, which had had an identical vaginal smear history, was menstruating from an 'interval' endometrium; there was no sign in this animal's ovaries that ovulation had occurred during the preceding two or three cycles. Laparotomies on other animals also showed that menstruation might occur without previous ovulation.

'Out of about twenty-seven cycles of which something is definitely known, from autopsy or exploration, ovulation has occurred in seven only . . . Histologically there are two types of menstruating endometrium—one showing “premenstrual” changes, the other devoid of them, according to the occurrence or non-occurrence of ovulation twelve or fourteen days beforehand.'

The same observation had been reported in the preceding year by Edgar
Allen of St Louis, who had also been studying the sexual cycle of the rhesus monkey (Allen 1926a). Three years before this, he and Edward Doisy had shown, on the basis of the vaginal cornification test, that the source of the oestrogenic (then called follicular) hormone in monkeys is the ovarian follicle. In experiments with this hormone, Allen (1926b) had also shown that if daily injections of oestrogen into spayed mature rhesus monkeys are suddenly discontinued, menstruation soon follows. He also found that the removal of both ovaries from a monkey towards the end of, or immediately after, the follicular phase of the cycle (as judged by the colour of the sexual skin) is followed by ‘apparently typical menstrual bleeding’ five to thirteen days before menstruation would be expected to occur. Allen therefore suggested that ‘menstruation is due to an absence of follicular hormonal stimulus after the hormone has been acting for a certain period of time’ (Allen 1927). The fact that menstruation is normally delayed for some two weeks after ovulation he explained as being due to the possible continued secretion of the follicular hormone (oestrogen) by the corpus luteum, and he suggested that the non-occurrence of menstruation during pregnancy might be due to the secretion of oestrogen by the placenta. Thus at that time Allen was assuming that the ‘mechanism’ underlying the process of menstruation is dependent on the action, and cessation of action, of oestrogen alone.

This hypothesis did not accord with the facts as they continued to emerge, and in 1929 the alternative explanation was suggested (Zuckerman 1929), that menstruation in cycles in which ovulation does occur represents a delayed breakdown of the pro-oestrous ‘interval’ endometrial growth that heralds ovulation, combined with the breakdown of the pseudo-pregnant growth that follows the same ovulation, and which is due to stimulation by the hormone of the corpus luteum. In cycles in which ovulation does not occur, menstruation represents only the delayed degeneration of the pro-oestrous endometrium, which is maintained for longer than it would otherwise have been by the continued secretion of a threshold level of oestrogen. The first experimental demonstration that progesterone could delay the onset of uterine bleeding, in accordance with this hypothesis, to which the authority of Corner’s name was soon added, was that of Philip Smith and Earl Engle in 1932. Later their findings were confirmed by F. L. Hisaw of Wisconsin (1935), and by Corner (45, 49) and S. Zuckerman (1935, 1936, 1937) who succeeded in reproducing all the phases of the menstrual cycle in spayed female rhesus monkeys by a judicious combination of injections of oestrogen and progesterone. As Corner relates in his autobiography (104),

'I first presented this modified hormone-deprivation theory at the annual meeting of the National Academy of Sciences in 1937 (Science, Volume 85, pp. 437–38) and expounded it fully the next year in the American Journal of Physiology (Volume 124, 1938, pp.
George Washington Corner

(1937) a conception of the antagonism
of progesterone to estrogen, in the primate cycle, practically identical
with mine. Solly and I, then as now cordial friends, had no reason to
contend for priority in this matter. So far as I know, the basic
hypothesis of an antagonistic effect of progesterone upon estrogen
has never been disputed; in fact, a good deal of evidence has
accumulated to support it, and the whole concept is now generally
accepted.'

Corner noted that this concept is basic to our understanding of the
mechanism of action of the birth-control pill.

By 1945, Corner’s time for laboratory research was being heavily
eroded by his executive duties as head of the Carnegie Laboratory, and by
his willingness ‘to give lectures, write reviews, and serve on committees,
all of which seemed to be part of a scientist’s duty’. He consequently
decided to consolidate all his own observations on the ovarian and uterine
cycle of the rhesus monkey in a major report entitled ‘Development,
organisation, and breakdown of the corpus luteum in the rhesus monkey’,
and in the preparation of which he was able to add relevant material lent
to him by Carl Hartman and George Bartelmez. He regarded this
monograph (61), which was published in his fifty-fifth year, as the cul­
mination of the 30 years he had spent in observation and experiment on
the female reproductive cycle.

The mammary glands

Because the corpus luteum degenerates as the period of gestation draws
to a close, Corner had deduced that ‘the onset of labour is caused, or at
least facilitated, by the cessation of progesterone action’. He also realized,
and then confirmed experimentally, that lactation itself could not be due
to the action of progesterone. When, during pregnancy, the corpora lutea
(or luteum) are actively producing the hormone, the growth of the
mammary glands is promoted, but since the corpora lutea degenerate
before parturition, they cannot be responsible for stimulating the
secretion of milk. Consequently Corner supposed that some unknown
hormone of the anterior pituitary (the adenohypophysis) might be
involved. Herbert Evans had already shown that this gland secretes a
hormone that can prolong the life of the corpora lutea of the rat. Could it,
therefore, also produce a hormone that stimulates lactation? In 1930,
working with E. P. Bugbee, a biochemist, Corner showed (29) that it
did; they were able to obtain a pituitary extract that stimulated lactation
in rabbits. Subsequently Corner found that the same effect had been
independently reported in 1928 by P. Stricker and F. Grueter working in
Paul Bouin’s laboratory in Nancy. But it was Corner’s work that
stimulated the subsequent enquiries by Oscar Riddle that led to the discovery of prolactin, and to its chemical isolation by Choh Hao Li of Berkeley.

OTHER SCIENTIFIC STUDIES

Although the main thrust of Corner’s researches were physiological, he never lost the interest in morphological embryology that had been stimulated in him by Franklin Mall. In addition to an investigation of early human embryos, some carried out in collaboration with C. H. Heuser, he joined forces with Carl Hartman (63) and G. W. Bartelmez (44, 75, 77) in studies of the segmenting ovum of the rhesus monkey, and of normal and aberrant corpora lutea in monkeys.

HISTORY OF MEDICINE

Corner punctuated his life as an experimental biologist with excursions into medical history, sometimes into the history of ideas and the development of trends, more frequently focusing on biographical studies of men he had known. His first major historical work, in the writing of which he had been encouraged and helped by Dr Charles Singer, was published in 1927 under the title Anatomical texts of the earlier Middle Ages (83). He never ceased to be fascinated by the history of the mediaeval Medical School of Salerno, about which he published several papers (86, 88, 89), but his main historical work related to the development of medical education and science in the United States, and on the contributions of particular individuals. Among the more significant of his writings on the subject was his annotated edition (90) of the Autobiography of Benjamin Rush, the outstanding American physician of the latter part of the eighteenth century, and one of the signatories of the Declaration of Independence. Corner’s experiences with the Grenfell Mission when a young medical man had also imbued in him a taste for the history of Arctic exploration, a taste that was reinforced by the story of one of his childhood heroes, Elisha Kent Kane, a Philadelphia physician who was the first American Arctic explorer of note. Soon after he became Executive Officer of the American Philosophical Society, he started to write a book about Kane. When he had completed his researches for the biography, and after a substantial part had been drafted, members of the Kane family presented to the Library of the Society a large mass of Kane papers that Corner had never seen before. He had to lay aside his manuscript, begin research anew, and rewrite his book—which was, of course, much richer for the unexpected appearance of so much new material (103).
As well as being a diligent and considerate university teacher, George Corner regarded it as his duty to try to educate a wider public about the facts of reproduction. The mores of the inter-war years were very unlike what they are now. Sex was a taboo subject, and considerable ignorance about the facts of reproduction prevailed in the general public, and particularly among young people. As a scholar of impeccable taste, Corner therefore frequently lectured on the subject to non-specialist audiences. He also wrote two simple books on sex, one addressed to boys (47) and the other to girls (50). From 1947, as Chairman of the National Research Council’s Committee for Research in Problems of Sex (he had been a member from 1934), he staunchly defended the work that Alfred Kinsey was carrying out into human sexual behaviour. Kinsey's studies were partly supported by the Rockefeller Foundation, and Mr Dean Rusk, then the Foundation’s President and later Secretary of State in both President Kennedy’s and President Johnson’s administrations, had become much worried by some of the adverse public reaction to what Kinsey was proclaiming. He therefore arranged for Corner to testify before the Un-American Activities Committee, which was then dominated by the notorious Senator McCarthy, to urge that there was nothing un-American in what Kinsey was revealing about the ways of the American male and American female. Corner was not called.

He was Secretary-Treasurer of the American Association of Anatomists for eight years, and then President for two. He was President of the American Association for the History of Medicine from 1954 to 1955. He was also Chairman of the International Committee on Anatomical Nomenclature during the 1950s, and President of the International Congress of Anatomists that convened in New York in 1960. In 1964 he served in the same capacity at the International Congress of Endocrinology that took place in England. He delivered the Terry Lectures at Yale in 1940 (52), the Vanuxem Lectures at Princeton in 1942 (56), the Addison Lecture at Guy’s Hospital in 1950 (68), and the Dale Lecture of the British Society of Endocrinology in 1964. His election in 1940 to both the National Academy of Sciences and the American Philosophical Society were the first of a series of distinguished honours, including many honorary degrees.

Corner’s friendly spirit never diminished as he grew in years and eminence. He was in his twenties before he broke with the ritual of daily prayer and with the nonconformist discipline in which he had been brought up, and which forbade alcoholic drink. But these relaxations in no way weakened the strong sense of purpose and duty which his powerful nonconformist upbringing had instilled in him. His family life was happy, and its even tenor was not broken until, after 50 years of marriage, Betsy, then 77, developed senile dementia and had to be confined to a
Sanatorium, where he visited her every week and where she died in her 85th year. The two had shared the grief of the loss of their only daughter Hester nearly thirty years before. Corner, now alone, continued with his work and his lectures, always sustained by his son, George Washington Corner IV, Professor of Gynecology at the University of Alabama in Huntsville, by his grandchildren, and by his numerous friends.

In 1978 Corner sat down to write his autobiography. It appeared in 1981, the year of his death, under the title The seven ages of a medical scientist (104). In his usual orderly way the author had lived long enough to correct the proofs, and to write, in a hand that shows no sign of age, inscriptions on cards for those of his friends to whom he wished the publisher to send copies. His card to me is inscribed to his 'oldest English friend' and in the book he refers to the 'most enduring friendship' which he made with me on his first visit to England in 1923. He was wrong about the year—it was later than that—but like all who knew him I cherish the memory of a man whose generosity of heart and honesty of purpose made him stand out through several generations.

My thanks are due to Mr J. Whitfield Bell, Jr, George Corner's successor as Executive Secretary to the American Philosophical Society; to the late Professor E. C. Amoroso, F.R.S.; and to Professor Graham Weddell, for reading my manuscript and for their helpful suggestions.

The photograph reproduced was taken by Fabian Bachrach of Philadelphia in 1969.

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