Edward Charles Dodds (1899-1973) [1]

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Edward Charles Dodds [3] researched the function and effects of natural and artificial hormones [4] on the endocrine system in England during the twentieth century. Though he first worked with hormones [4] such as insulin, Dodds focused on the effects of estrogen [5] in the body and how to replicate those effects with artificial substances. In 1938, along with chemist Robert Robinson, Dodds synthesized the first synthetic estrogen [6] called diethylstilbestrol. Despite the wide use of diethylstilbestrol to treat a variety of hormonal problems like miscarriages during pregnancy [7] and menopause, Dodds argued against the use of synthetic substances in the human body due to their unknown effects. Just before Dodds's death, his hypotheses were confirmed when researchers showed that people exposed to diethylstilbestrol often developed cancer. Dodds was one of the first researchers to investigate the endocrine or hormone [8] system in humans [9], and his research led to the creation of other synthetic hormones [4] used in contraceptive pills and hormone [8] replacements.

Edward Charles Dodds [3] was born on 13 October 1899 in Liverpool, England, to Jane Dodds and Ralph E. Dodds. His mother came from a wealthy family that helped support her and her husband and later Dodds's career. His father was a businessman in retail footwear and his unsuccessful shops often required the family to move. Shortly after Dodds was born, the family moved to Leeds, England, and later on to Darlington, England, where Dodds spent his early childhood. In 1910, the family moved again to Chesham, England, before finally settling in London, England.

Dodds began his education at the Harrow County School for Boys in Middlesex, England, in 1911. During his first year at Harrow, Dodds won many academic awards and played the role of Bottom in his school's production of Shakespeare's *A Midsummer Night's Dream*, for which a local newspaper praising his performance. After graduating from Harrow in 1916 at the age of seventeen, Dodds studied at Middlesex Hospital Medical School [10] in Middlesex. In 1917, he joined the London University Officer Training Corps to fight in World War I [11], where he contracted severe pneumonia and returned to medical school the following year.

In 1918, Dodds's father could not pay his medical school tuition because his business had failed. To continue his education, Dodds took a loan from his maternal uncle and became a tutor and teaching assistant for Alexander Kellas, a chemist who studied respiration in Middlesex Hospital Medical School [10]. Much of Dodds's research at this time dealt with respiration and the amount of carbon dioxide in the digestive system. In 1919, Dodds passed his preliminary medical exams with distinction in both physiology and pharmacology. Afterwards, he began assisting Swale Vincent, a physiologist at the Middlesex Hospital Medical School [10] who studied the organs involved in internal secretions, later called hormones [4].

In 1920, Middlesex Hospital appointed Dodds as an assistant in chemical pathology under Ernest Kennaway, who studied chemicals that cause cancer (carcinogens). Dodds replaced Kennaway as professor of biochemistry a year later, and that same year, he qualified as a member of the Royal College of Surgeons and became a licensed physician of the Royal College of Physicians, both in London. Dodds received a Bachelor of Medicine from London University in London. In 1923, he married Constance E. Jordan. They had one son, Ralph J. Dodds.

In 1924, Dodds and some of his colleagues published "The Distribution of Insulin in Human and other Animal Tissues, with a Description of a Micro-Method for the Estimation of Insulin in Tissues." The article compared methods for preparing and purifying large quantities of the hormone [8] insulin from different animals like sheep [12] and horses. Insulin is a chemical in the body that regulates metabolism by controlling when glucose is broken down for energy or stored as fat. Claude Bernard [13] who'd studied physiology in nineteenth century France, had hypothesized that chemicals functioned in the body to maintain homeostasis, a process organisms used to maintain stable physiological conditions. In 1874, William Gull in England had shown that damage to the thyroid gland and subsequent lack of thyroid hormones [4] in the body caused severe health problems.

In 1924, Dodds and George Beaumont, another physician at the Middlesex Hospital, published *Recent Advances in Medicine*. The book detailed research in medicine related to genetics, the thyroid, and other infections accompanied by illustrations. Dodds graduated with his doctorate in January of 1925 from the University of London in London, and six months later also completed his MD. That year, Dodds became the director of the Courtauld Institute and chair of biochemistry at the Middlesex Hospital. As chair, Dodds began working with hormones [4], publishing on the actions of ovarian hormone [8] in 1925 and the parathyroid hormone [8] in 1926.

In 1927, Dodds became the first director of the Institute of Biochemistry at Middlesex Hospital. In 1928, George Frederick Ernest Albert, King of the United Kingdom and the British Dominions and Emperor of India, became ill with blood poisoning. The king's physician called Dodds to help treat the king. Dodds helped to save the king's life. In return, the king awarded Dodds a membership to the Royal Victorian Order in 1929.

In 1932, at the request of the Middlesex Hospital benefactor, Samuel Courtauld, Dodds toured a variety of laboratories and clinics in the United States, including the Rockefeller Institute [14] in New York City, New York, and the Mayo Clinic in Rochester, Minnesota. Dodds used what he saw in the United States to improve the Institute of Biochemistry in Middlesex by setting up new wards to measure patients' metabolic rates, and by establishing new nursing facilities.

From 1927 to 1932, Dodds researched female sex hormones [15] and their preparation in the laboratory. At that time, biologists had already identified estrogen [5] as a naturally occurring hormone [8], secreted by the ovaries, and had determined some of the effects estrogen [5] had on ovarian function. Estrogen is one of the primary female sex hormones [15] responsible for the production of eggs (ova), ovulation [16], and conception [17]. Dodds wanted to synthesize estrogen [5] in the laboratory to use it to treat many conditions caused by a lack of estrogen [5], like various cancers and difficulties in getting pregnant.

In 1891, Alexander P. Dianin in Saint Petersburg, Russia, had synthesized the first synthetic estrogen [6], bisphenol A [18] (BPA). But researchers hadn't shown its estrogenic effects until 1932, when Dodds examined it in the lab. In 1934, Dodds synthesized another, more stable form of synthetic estrogen [6], showing that his synthetic estrogen [6] could trigger the same reactions in animals as natural estrogen [5]. Dodds's breakthrough came in 1938 when he began working on the synthesis of estrogen [5] with Robert Robinson, head of Oxford University's Dyson Perrins Laboratory in Oxford, England. During this partnership, a chemist working under Dodds, Wilfred Lawson, wrote a chemical formula for an artificial estrogen [5]. Around the same time, Oxford student Leon Goldberg synthesized the compound diethylstilbestrol (DES), called stilbestrol in England. In 1939, the Medical Research Council [19] in England approved DES to treat a variety of female reproductive problems including the absence of menstruation [20] (amenorrhea), pain during menstruation [20] (dysmenorrhea), and several menopausal disorders. The Food and Drug Administration [21] in the US approved the drug in 1941 for similar uses. A year before, Dodds showed that by administering DES to rabbits and rats he could prevent and terminate pregnancies, a capacity that led to the drug later being used as an emergency contraceptive.

Dodds claimed that his intent in synthesizing DES was theoretical. His biographer, Dickens, claims that Dodds just wanted to see if hormonal reactions in the body could be caused by synthetic chemicals. In 1949, researchers Oliver Watkins Smith and George V. Smith in the US showed that low estrogen [5] levels correlated with pregnancy [7] complications like miscarriages and premature delivery. Smith and Smith suggested that treatment with synthetic estrogen [6], like DES, could prevent those pregnancy [7] complications. Though in 1938 Dodds had shown that DES caused miscarriages in rabbits and rats, the Smiths' results prompted the drug's use as a method for preventing miscarriages in the US and Europe. Dodds argued against the use of any sort of synthetic or artificial hormone [8] in the female reproductive system, which according to him is too sensitive for such treatments. He further argued against the use of DES as an emergency contraceptive and miscarriage [22] preventative.

In his later years, Dodd's researched how other chemicals influenced endocrine systems, and he served on a variety of professional boards and organizations. From 1947 to 1949, Dodds served as master of the Worshipful Society of Apothecaries of London. In 1949, he became a member of the National Research Development Corporation, a corporation focused on commercializing public funded innovations in England and later called the British Technology Group. In 1964, Dodds was knighted. From 1962 to 1977 he served as president of the Royal College of Physicians in London, England and in 1964, he was given a baronetcy.

In 1969, Dodds's wife died. Two years later, in 1970, researchers Arthur Herbst [23] and Robert Scully [24] in the US showed that female fetuses exposed to DES *in utero* developed clear cell adenocarcinoma, a vaginal cancer. Dodds's son claimed that reports about that research misrepresented Dodds, and that Dodd's had never intended DES to be used as a drug. Dodds died on 16 December 1973.

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Subject

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