

# Sir Graham Collingwood Liggins (1926–2010)

Sir Graham Collingwood Liggins devoted much of his professional life to obstetric research. Liggins demonstrated that hormones created by the fetus, rather than hormones solely from the mother, helped initiate labor. Liggins also discovered that cortisol given to pregnant mothers helped delay premature labor, and that it increased the likelihood that premature infants would breathe normally after birth. Prior to cortisol treatment, premature infants often died of respiratory distress syndrome characterized by the inability to inflate immature lungs. Before the clinical application of Liggins's discoveries in the 1980s, premature infants born before 32 weeks of gestation generally died because of respiratory distress.

Liggins was born 24 June 1926 in Thames, New Zealand, a twin to his sister Elizabeth and a brother to three other siblings. Liggins was the last child born to his mother Isobel and father James Liggins, a surgeon. By the age of three Liggins preferred to be called Mont after the cartoon character Monty Mouse, a nickname that lasted Liggins's lifetime. Liggins wrote about his adventures as a boy, scouring hillsides around Thames, exploring old mines and on one occasion, blowing up dynamite found during his explorations.

At the age of fifteen, Liggins moved from Thames to Auckland, New Zealand, to attend Auckland Grammar School for his final year of high school. Upon graduating, he entered Auckland University in Auckland, New Zealand, where he earned an undergraduate degree in pre-medical studies in 1944. Liggins then attended Otago Medical School in Dunedin, New Zealand, where he graduated with a Bachelor of Medicine and Bachelor of Surgery in 1948. Liggins then interned as a surgeon in Auckland, and upon completing his internship he was a general practitioner in Hamilton, New Zealand, for two years. During this time, Liggins saved enough money to travel to London, UK, for specialist training in obstetrics and gynecology. Liggins arrived in the UK in 1953, and a year later married a classmate, Celia, who would later become Auckland's first female obstetrician. After six years in the UK, Liggins returned to New Zealand with his wife, two daughters, and a son. Their second son was born two years later.

Upon his return to New Zealand, Liggins worked as an obstetrician at the National Women's Hospital in Auckland, where he met A. William Lilley, a fellow obstetrician who would go on to perform the world's first intrauterine transfusion to prevent Rhesus disease in 1963. Discussions with Lilley prompted Liggins to focus on preterm labor in women, using pregnant sheep as a model organism. While on sabbatical in 1960, Liggins studied veterinarian medicine at the University of California at Davis in Davis, California. While there, Liggins learned more about the physiology of lambs in utero by removing the pituitary gland from lamb fetuses. After removing the fetal pituitary glands, Liggins observed that pregnancy in the mother ewes continued far beyond term.

Liggins hypothesized that the hormone cortisol, regulated in part by the fetal pituitary gland, may be responsible for the delay in labor. Once Liggins returned to Auckland, he began studying the effect of cortisol injections on pregnancy when lamb fetuses had their pituitary glands excised. When the fetal pituitary gland was removed and cortisol was artificially injected into the fetus, the pregnant ewes generally gave birth two days after the injection. Liggins inferred that the initiation of labor was due in part to the cortisol produced by the fetus' pituitary glands, rather than by hormones produced by the mother. Therefore, the relationship between the fetus and cortisol is one part of the physiological mechanisms that initiate labor.

During those experiments, Liggins also noticed that the premature fetal lambs could breathe following the cortisol treatments, when normally their lungs would have been too underdeveloped to breathe and thus causing the lambs to eventually die. Liggins suspected that the cortisol induced

an enzyme which promoted surfactant synthesis. Surfactants are lubricants that prevent the collapse of lung tissue by lowering the surface tension of lungs when expanded. Fetal lungs do not begin to produce surfactant until the last three to four weeks of pregnancy. In premature fetuses, the lack of surfactant does not allow the alveoli of the lungs to expand very well, so oxygen cannot be absorbed into the blood stream. Poor breathing and oxygen absorption is also called infant respiratory distress syndrome, which generally leads to death.

Interested in transferring his knowledge of cortisol in sheep to humans, Liggins worked with Ross Howie, a pediatric specialist, to organize a double blind trial focused on the relationship between corticosteroids and accelerated lung maturation in premature infants. The trial revealed that significantly more neonates survived from women who began labor prematurely and were treated with corticosteroids than did neonates from women who began labor prematurely and weren't treated with corticosteroids. Early neonatal mortality was 3.2 percent in the treatment group but was 15 percent in the control group. Liggins and Howie published their results in 1972. Many ignored the work, in part because smaller studies had not shown a similar benefit, but as other researchers would later recount, the small island nation of New Zealand was not a hub of globally significant medical research. By the 1980s Liggins' corticosteroids treatment for premature infants became commonplace in hospitals, preventing many instances of respiratory distress syndrome and saving the lives of many premature infants.

In 1971, Liggins became a professor in obstetrics and gynecological endocrinology at the University of Auckland. In addition to obstetrics, Liggins studied the physiology of diving seals off the coast of Antarctica in the late 1970s, and discovered that elevated cortisol levels helped seals hold their breath under the high pressures caused by their deep sea diving. Liggins was elected as a fellow of The Royal Society of London in 1980 for his scientific contributions, appointed Companion of the British Empire in 1983, and knighted in 1991. Liggins retired from clinical practice and from his position as department chair in 1987. In 2001, the University named its biomedical and clinical research center, the Liggins Institute.

Liggins died on 24 August 2010 in Auckland after a lengthy illness. Peter Gluckman, the Chief Science Advisor to the New Zealand Prime Minister, and once a junior researcher in pediatrics and developmental physiology under Liggins, noted that Liggins was a meticulous scientist that possessed the ability to bridge the gap between animal and human research.

## Sources

1. Gluckman, Peter. "In Memoriam: Sir Graham (Mont) Liggins FRS:" Eulogy by Professor Sir Peter Gluckman, FRS, August 28, 2010.
2. "Graham Collingwood (Mont) Liggins," *The New Zealand Medical Journal* 123 (2010): 107-8.
3. Liggins, Graham Collingwood, and Ross Howie. "A Controlled Trial of Antepartum Glucocorticoid Treatment for Prevention of the Respiratory Distress Syndrome in Premature Infants," *Pediatrics* 50 (1972): 515-25.
4. "Sir Graham Collingwood Liggins," *New Zealand Listener*, September 10, 2010, <http://medicalalumn.otago.ac.nz/> (Accessed April 9, 2011).
5. Thorton, Jim. "Sir Graham 'Mon' Liggins Obituary," *The Guardian* September 6, 2010. <http://www.guardian.co.uk/society/2010/sep/06/sir-graham-mont-liggins-obituary/print> (Accessed April 9, 2011).
6. Watts, Geoff. "Graham Collingwood Liggins," *The Lancet* 376. (2010): 1140.
7. "Sir Peter Gluckman, Prime Minister's Chief Science Advisor on the Death of New Zealand's Outstanding Medical Scientist, Sir Graham Liggins" Office of the Prime Minister's Science Advisory Committee Media Release, August 24, 2010.