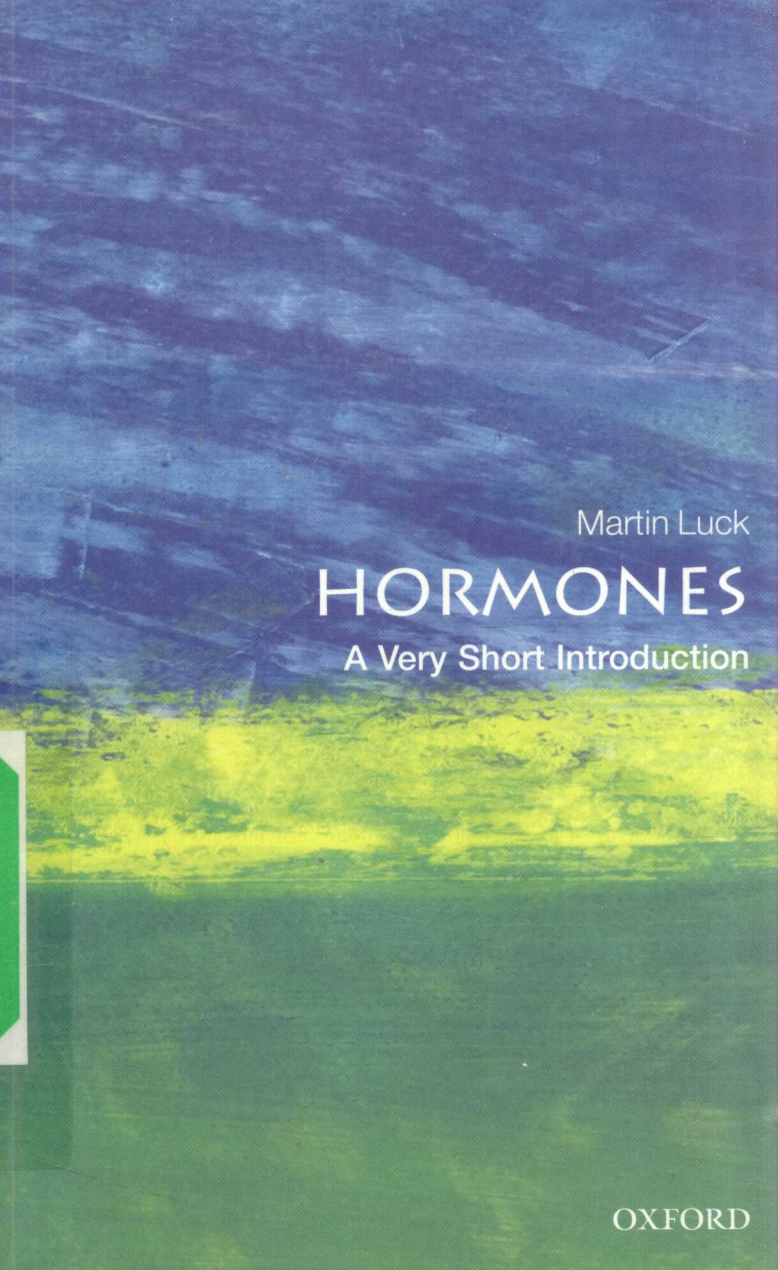
Martin Luck
HORMONES
A Very Short Introduction
OXFORD

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For Jacob
whose life will be completely different from mine

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Chapter 1
Hormones, history, and the shoulders of giants

A matter of size

The parish register of St Anne's Church, Sutton Bonington, a Leicestershire village a couple of miles from where this book is being written, records the following death: '1773 Feb. 7th William Rice [or Riste], aged 30, seven feet four inches high.' According to village history, this 'Giant of All England' was exhibited about the country and George III gave him a suit of scarlet silk. He reputedly grew by six inches each year between the ages of 14 and 21. He was buried in the chancel of the church, his corpse being carried by eight men with eight maids bearing the pall. Upwards of 500 people attended. No sign of his grave remains but there was once a peg high up on the chancel wall on which he hung his hat.

One's view of William depends on one's interests. Village folk are presumably grateful to have a noteworthy character in their heritage, whilst historians might check the veracity of the facts reported about him. To sociologists he represents minor 18th century celebrity, whilst psychologists may wonder how he coped with constant attention and royal interest. Engineers might calculate the loads on the arms of the coffin carriers. Compilers of lists would find that although William was very tall, he holds no record: Robert Pershing Wadlow of Alton, Illinois who died in

1940 aged 22 years was 2.72 metres or 8 feet 11 inches and would have hit his shoulder on William's hat peg. Statisticians might be interested to know whether taller people have shorter lives. Doctors would want to ameliorate any height-related illnesses and seek ways of preventing the condition in others.

Anyone interested in hormones would immediately want to know if William, and indeed Robert, suffered from too much or too little of something. Many hormones influence growth and although we cannot be certain why these individuals grew so tall, we can consider some possibilities.

From being an average sized teenager, William seems to have experienced an unusually rapid growth spurt, nearly doubling his length in about seven years. Growth hormone (GH), which is produced by the pituitary gland, drives the growth of children and adolescents. Perhaps William's pituitary secreted an unusually large amount of GH at crucial stages in his life. This might indicate something wrong with the gland itself or that it was being overstimulated by his brain. The part of the brain called the hypothalamus controls much of what the pituitary does, including its production of GH. It both stimulates it, by the eponymous growth hormone releasing hormone (GHRH), and inhibits it, with the less obviously named Somatostatin. The balance between these influences decides the outcome.

Alternatively, William's secretion of GH could have been normal but perhaps his liver responded by secreting too much insulin-like growth factor I (IGF-I). This hormone does the operational work of the growth system, causing bones to lengthen and muscles to build. It also raises the body's rate of metabolism to keep pace with everything. Normally, IGF-I suppresses the secretions of the pituitary gland and hypothalamus. This sets up a correction system so that the amount of GH in the blood becomes self-adjusting. So yet another possibility is that William's pituitary or brain was just insensitive to IGF-I and he did have too much GH after all.

William eventually stopped growing but evidently did so rather late. Adolescents normally reach maximum height in late teen age because the sex hormones testosterone and oestrogen, produced by their increasingly active gonads, irreversibly alter the structure of limb and other long bones. A bone grows from its two end regions, called epiphyses (sing. epiphysis). These regions have cells that respond to IGF-I by dividing and producing cartilage. The cartilage gets smeared on the ends of the shaft, making it longer, and then becomes calcified into hard bone.

Sex hormones encourage this lengthening during the mid-teenage growth spurt but they eventually cause the epiphyses to fuse with the rest of the bone (called epiphyseal closure), thus preventing further elongation. So perhaps William's testes matured late and the slow build up of testosterone allowed his bones to lengthen for a little longer than usual.

What happens if there is too much IGF-I after limb bone growth is complete? This can happen if the pituitary develops a GH-producing tumour, and it produces the characteristic signs of a disease called acromegaly. The liver responds to the increased GH by producing too much IGF-I and bones in all parts of the skeleton become thicker and wider, rather than longer. The jaw and brow may become heavy. The hands, feet, and digits may become disproportionately large. In the days when men wore hats most of the time, an unexpected need for a larger one might be the first sign of this rare condition.

We have no information about William's facial features, nor about the size of the hat he threw on the chancel peg each Sunday, so we have no evidence of a tumour. Nor can we guess at his testicular development (the female attention at his funeral notwithstanding). There are other hormones that influence body growth, including cortisol (produced by the adrenal glands) and thyroxine (from the thyroid gland). Unusual amounts of these

may have contributed to William's condition, although in that case history might have recorded some other characteristic features to give us a clue.

We cannot be sure why they grew so fast but William Rice, Robert Wadlow, and other giants represent one end of the bell curve of human heights. At the other end, there are exceptionally short individuals whose limited stature can also have a hormonal explanation. Height is partly an inherited characteristic but its genetics are extremely complex. No single gene has an overriding influence. In any case, genes do not determine characteristics—they just provide opportunities for other factors to act. Our friend William, however much GH or IGF-I he had in his blood, would not have grown so tall had his diet not given him sufficient energy and protein to do so.

We notice very tall and very short individuals because they are exceptions. Yet each of us has a unique body conformation, encompassing much more than just our height. This reflects our individual biological history. Nutrition and disease, especially during childhood and adolescence, have a large part to play. Height, weight, and aspects of health are also affected by the health, nutrition, and age of our mother during pregnancy, and probably by the circumstances of our grandmothers during their pregnancies too. Thus we inherit our bodies in an environmental as well as a genetic sense. Unusual amounts of hormones, occurring for reasons that may be ultimately unclear, impose further variations and contribute to our individuality.

Even though individual extremes of height seldom have a simple genetic cause, there are some examples of clearly inherited height difference. The Efe of Northeastern Democratic Republic of Congo are the shortest of any human population, with an average male height of 143 cm (4ft 8in). The height differential when compared to reference humans is detectable at birth and increases up to the age of 5 years.