

# One hundred years of hormones

Tom Parkhill, Society for Endocrinology



In 1903, Ernest Starling and his brother-in-law, William Bayliss, were repeating Pavlov's (of Pavlov's dogs fame) experiments on secretion of digestive juices into the gut. Pavlov believed that secretion was solely under nervous control, but Bayliss and Starling showed that a circulating factor, which they called secretin, also played a part. Over the next couple of years, it became obvious that secretin was one of a class of factors which are released into the bloodstream and stimulate activity in a different part of the body. Over dinner at Caius College, Cambridge, Starling and the distinguished biologist William Hardy pondered what they might call these new circulating factors. A classical colleague, W T Vesey, produced the Greek verb for "excite" or "arouse". In July 1905, Starling first used his new word in the Croonian lectures at the Royal College of Physicians, *'These chemical messengers, however, or hormones (from ὁρμάω, I excite or arouse) as we might call them...'*

A hundred years on, hormones are centre-stage. Most non-scientists might not know exactly what a hormone is, but the concept of a chemical surging through one's body is familiar to everyone, and terms such as testosterone and adrenalin are in everyday use.

We now understand how hormones rule our lives. They determine our mood, our weight, when we go through puberty, how aggressive (or awake) we feel, our stress levels, and how strong our bones are. They control our sugar

and water balance. They determine whether we will grow to normal height, become fantastically tall or remain very short. They regulate our reproduction and wreck our adolescence. At the same time, there are important areas of endocrinology where a better understanding is beginning to allow us to take control, and where the practical use of the science will allow us to make decisions which will affect not only our own individual lives, but perhaps even the lives of future generations.

## A growing problem

The frightening increase in the levels of obesity and type 2 diabetes (where your body does make insulin, but doesn't respond to it properly, ie becomes insulin resistant) is one of the great public health challenges of the twenty-first century. Almost two thirds of UK adults are now overweight or obese, and obesity is one of the main risk factors for type 2 diabetes; as the level of obesity rises, so does the incidence of type 2 diabetes. Diabetes UK estimates that there are approximately 1.8 million people in the UK with confirmed diabetes, with up to a million more who have undiagnosed type 2 diabetes. The diabetes epidemic means that, internationally, we are seeing a doubling of the incidence of diabetes every generation. Controlling how the population gains weight and understanding why this leads to diabetes underlies much of the current work on the prevention and cure of diabetes and obesity. From work on islet cell

transplantation, to elucidating the mechanism of insulin resistance, to work on how hormones control our appetite, hormones are central to tackling the problem. For example, there's a significant amount of work under way into how the hypothalamus secretes hormones that control our appetites. UK researchers are amongst the world leaders in the development of hormonal methods of appetite control.

## To HRT or not to HRT?

In 2002, the US National Institute of Environmental Health Sciences labelled steroidal oestrogen a "known carcinogen", which was probably a shock to the more than 30 million Americans taking hormone replacement therapy or the contraceptive pill. Around 3.5 million British women use the pill at any one time, and the Royal College of Obstetrics and Gynaecology estimated in 2002 that around a third of British women in the 50-64 age group were taking HRT. The publication of the US *Womens' Health Initiative Study*, followed by the British *Million Women Study*, changed everything for HRT. The realisation that HRT increases the risk of breast cancer led to large numbers of women discontinuing post-menopausal HRT. However, HRT is still a valid treatment in many circumstances, and the supply of reliable information reaching the public has been far outstripped by an avalanche of HRT scare stories in the last three years. The average GP, never mind the woman in the street, is confused by the deluge of

contradictory information. The Society for Endocrinology believes that the lack of good information on HRT for the public has been one of the failures of the medical community and the government over the last three years, and this needs to be addressed.

### The declining male?

Oestrogens, or at least oestrogen-like compounds, are also present in our environment. The last 20 years have seen increasing evidence on hormonally-active substances disrupting natural ecosystems. In the late 1960s it was found that female whelks had developed male characteristics, especially if they were in proximity to the antifouling agent tributyl tin. The example that probably first hit the international headlines was the decline of the Florida alligator population, believed to be due to endocrine disruption. But there is ample evidence of endocrine disruption even in British freshwater fish populations. So far, there's limited evidence that this endocrine disruption is causing problems in the human population, but of course this needs to be closely monitored, especially in the light of the rapidly decreasing male sperm counts observed in recent decades.

### The emancipated female

Hormone treatments in the last hundred years have led to control of type 1 diabetes, thyroid conditions, pituitary conditions, and many other potentially fatal or debilitating conditions, but the best-known successes of endocrinology in recent years are probably in reproduction and oncology. A world without the contraceptive pill (first used in 1956) would be very different to the one we know today. Many researchers are now working towards development of a "male pill", and most activity centres around finding the right combination of hormones to eliminate fertility while maintaining libido.

### Hormones and cancer

Cancer treatment has been revolutionised by the understanding of the role of hormones and growth factors in cancer development and progression. Tamoxifen, which helps slow the growth and reproduction of breast cancer cells by blocking oestrogen in the breast, was developed in the UK, and is one of the great triumphs of British endocrinology. Now, new drugs such as aromatase inhibitors and SERMs (tamoxifen is a SERM) hold out the prospect of not only controlling breast cancer, but also preventing it in those most at risk. The substantial reduction in mortality from breast cancer has to be one of the main medical achievements of the late twentieth century.

### The next hundred years

In her recent book, *The Truth About Hormones*, journalist Vivienne Parry estimated that a quarter of all Nobel prizes in medicine and physiology in the last 35 years have been awarded in endocrinology. Given the quality of current research and the range of topics it covers, this could easily be exceeded in the next 35 years.

In many ways, the challenges in endocrinology are the same as in many other areas of British science and clinical practice. We need more good young scientists to take up the discipline, and then we need to keep them both in research and in the UK. There is a frightening lack of good young endocrine scientists to replace the current generation of senior scientists, and this will not change until there are better and clearer career structures – scientists with young families do not want the insecurity of repeated 2-3 year grants on low salaries. In clinical endocrinology, there are similar issues in terms of attracting top young doctors into an academic discipline such as endocrinology. The current UK training system

makes it less attractive to opt for a career in clinical research.

Another issue for parliamentarians is that many of the major medical issues of the twenty-first century, such as obesity and osteoporosis, are being dealt with on a fragmented basis. For instance, osteoporosis research and care can take place in endocrinology, rheumatology, gerontology etc, with sometimes little co-ordination, despite the fact that most new developments are endocrine in origin.

Many endocrine diseases are comparatively rare, and also complex, and need to be treated in specialist centres, where surgeons see many cases each year and physicians are involved in current research. For instance, in an article in the *British Medical Journal* in 1999 Clayton and colleagues demonstrated that surgeons in specialist centres obtain substantially better results in the case of pituitary tumour operations. It is important that the current moves towards care at community level do not prevent patients with rare and complex diseases being managed by appropriate specialists. Pavlov received the 1904 Nobel prize for his work on nervous secretion in the gut. As Pavlov went on to become famous for his later work on conditioned reflexes, his work on gut secretion became comparatively neglected. But it was Starling's discovery of hormones that came to influence all our lives.

### References

- The Truth About Hormones, Vivienne Parry, Atlantic Books (2005)
- Henderson J, Ernest Starling and "Hormones": an historical commentary, *Journal of Endocrinology* (2005) 184, 5-10
- Clayton R et al, Pituitary Surgery for Acromegaly, *British Medical Journal* (1999) 319, 588-589

### Where to find out more:

The Society for Endocrinology is commemorating the hormone centenary through a special website, [www.100yearsofhormones.org](http://www.100yearsofhormones.org). The site contains an article on the history of endocrinology as well as a series of "Starling Reviews", which look at important issues in endocrinology in the foreseeable future. *The Endocrinologist*, the newsletter of the Society, also contains an article on "Ten hot hormones", a brief introduction to some of the hormones which are currently attracting most research attention (<http://www.endocrinology.org/sfe/endocrinologist/end07508.pdf>). If you'd like to receive regular copies of *The Endocrinologist*, or if you want more information on endocrinology, contact Tom Parkhill or Jo Thurston on 01454 642206, [info@endocrinology.org](mailto:info@endocrinology.org).