

Historical Landmarks in Endocrinology and Diabetes

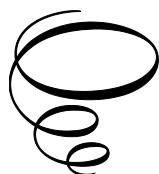
Historical Landmarks in Endocrinology and Diabetes:

The Fascinating World of Hormones

Edited by

Bayar A Qasim

**Cambridge
Scholars
Publishing**



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TO MY MOTHER, WHOSE AFFECTION SHAPED ME

TO MY WIFE, FOR HER UNWAVERING SUPPORT

TO THE MEMORY OF MY FATHER,
WHOSE WISDOM GUIDES ME STILL!

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PREFACE AND ACKNOWLEDGEMENTS

Today, the literature on endocrinology as a new branch of medicine is immense but also confusing in the wealth of information. To simplify the readers' view of this amazing juvenile field and bring their ideas together to form a vivid picture of the labour and hard work done to give birth to and develop this everlasting field, we saw it necessary for a history work such as this to be picked up and studied by audiences around the world.

I have been inspired and driven by this field all my academic and professional life, always eager to unravel and eager to share, and I hope to instill in you some of the magic endocrinology has instilled in me! Despite its relatively recent and fresh ascension into the ranks of medical branches, the historical development of endocrinology is very exciting. For quite some time, I looked up topics around the field of endocrinology, and it wasn't hard for me to know that a work on the milestones and landmarks of endocrinology would be a refreshing read for admirers of hormones and the history of medicine in general. Writing the book has been a laborious but worthwhile journey. We aim to deliver a book that makes it hard for readers to put down, a book that makes the reader want more and know more.

In this book, we highlight historical landmarks in endocrinology and diabetes. It primarily aims at inspiring those working in these medical fields, whether they are doctors, nurses, researchers, scientists, or those who just work with hormones in labs. This book is written around real endocrinological characters and events and uses art, such as paintings, as historical evidence. *Historical Landmarks in Endocrinology and Diabetes* combines endocrinological tales featuring historical odd practices, trial and error, but also flashes of brilliance and relentless determination, ultimately giving rise to the field of endocrinology.

This book would not have been possible without the collaboration and resilience of contributors who shared my passion for this work. Their contributions to the book are not simply confined by their writing roles but also by their support, guidance, feedback, and suggestions, which exceeded my expectations as the leader of this group. I recognise their efforts, advancements, and feedback, and I greet them with my warmest, most

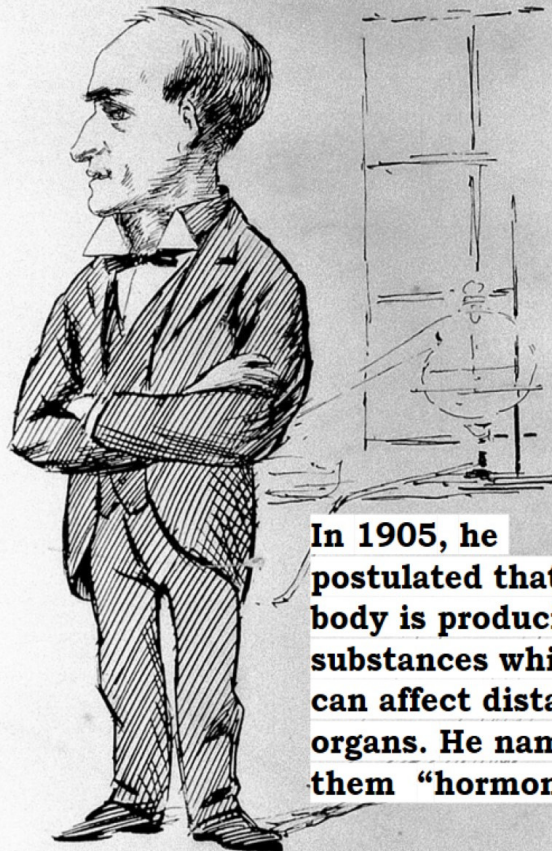
sincere gratitude. I wish them a bright horizon in their profession and future work.

Here I want to offer deep gratitude to Ms. Estela Dukan, assistant librarian at the Library of the RCPE—Scotland's oldest medical library. Ms. Estela Dukan offered great help in providing books and resources that were used throughout this book, and I am thankful to the fullest extent for her cooperation.

I would also like to extend my gratitude to the organisations from which I sourced images, artwork, and photographs for this book. Throughout the process, I had the pleasure of contributing to the design and editing of these images with the aim of complementing the text to enrich and convey key concepts effectively. Furthermore, I occasionally incorporated independent images to illustrate certain points, even if they were not directly related to the topics in the chapters. I hope you will find my efforts worthwhile, engaging, and informative.

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Ernest Starling
(1866-1927)
British Physiologist

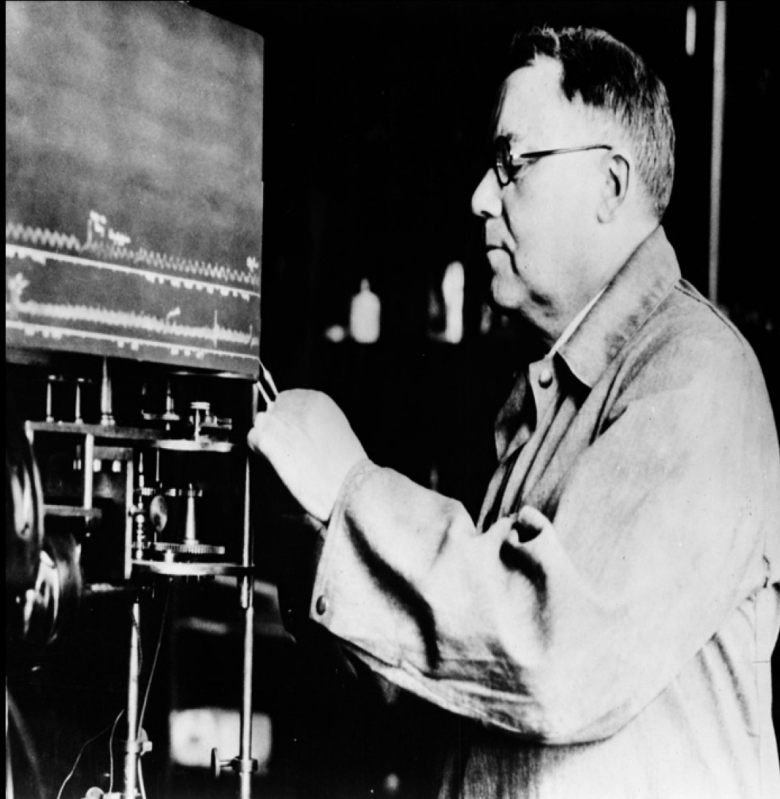


In 1905, he postulated that the body is producing substances which can affect distant organs. He named them “hormones”.

CARTOON No. 6.
THE STARLING.

Walter B. Cannon
(1871-1945)
American Physiologist

The Fascinating World of Hormones



“Agents which can determine whether an individual shall be a giant or a dwarf, an idiot or a normally intelligent person, a ‘sissy’ or a real male, a bearded lady or a woman; agents which are essential to normal metabolism-indeed, whose destruction may lead promptly to death-must evidently be respected”.....**Cannon, 1927**

Walter Bradford Cannon. Photograph. Public Domain Mark. Source: Wellcome Collection

CHAPTER ONE

HISTORICAL LANDMARKS OF NEUROENDOCRINOLOGY

SARA O. YOHANA AND RENDE S. KOCHARY



Pituitary Gland: “The leader of the endocrine orchestra.”

— Sir Walter Langdon-Brown, 1931.

Introduction

The ductless gland, or the hypophysis cerebri, were some of the names used to describe the pituitary gland. Hypophysis is a Greek term meaning ‘lying under’, receiving this name due to its position being under the brain. The term ‘pituitary’ comes from the Latin word pituitarius, meaning ‘phlegm.’ This was because, in earlier centuries, anatomists used to believe that mucus was brain waste secreted from the pituitary gland into the nasal cavities.

In the mid-1900s, the role of the hypothalamus in conducting the activity of the pituitary gland was discovered. The chemical messengers released from the pituitary gland communicate with various target organs in the body. Any disturbance in these signalling pathways can lead to disorders causing systemic changes in the body and clinically distinct features. Before the advancements in technology, little was known about this mysterious gland, which hid beneath the brain, but it would soon arouse the curiosity of physicians and surgeons alike after an association was found between this gland and the clinical findings of acromegaly by Pierre Marie in 1886.

Prior to the advancements and developments in science, patients with acromegaly were regarded as a sight to be seen—often exhibited as part of shows and circuses, or their skeletons used as displays in museums. Conversely, people with short stature were also regarded as abnormal creatures in ancient history, and would often be displayed as a source of humour in shows and exhibitions. Studies, research, and autopsies done on the bodies of patients with acromegaly would be the starting point of the discovery and isolation of the human growth hormone, which would provide a foundation for the treatment of certain endocrine and paediatric disorders.

Due to the gland being concealed deep within the brain, the disorders caused by the pituitary gland would have an unknown aetiology until the discovery of the individual hormones. For example, although cases of prolactinomas were described in writings back in the 16th century, the hormone prolactin itself wasn’t discovered until the 1900s.

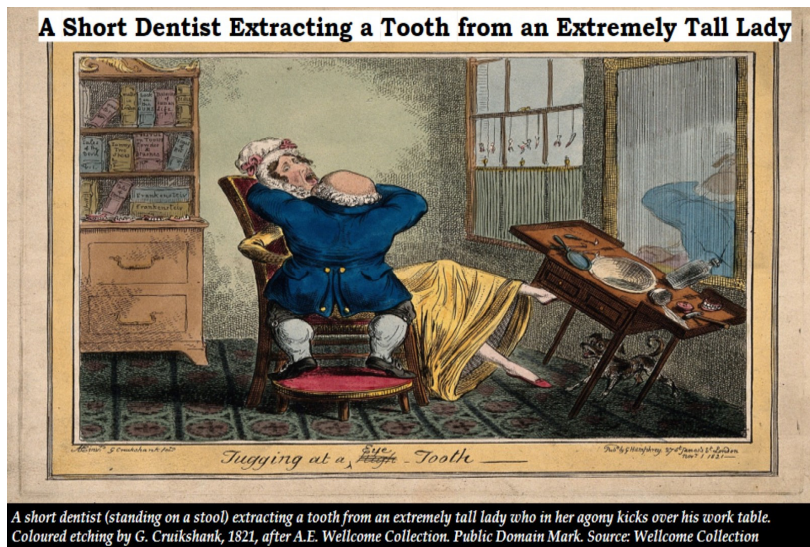
The discovery of other hormones, such as vasopressin, would also be delayed compared to the initial mention of the disorders they caused due to the scarcity of medical advancements. For instance, diabetes insipidus was first described as a clinical condition of polyuria and polydipsia and was differentiated from diabetes mellitus by differences in the taste of the urine in each of these conditions. The association between diabetes insipidus and

the pituitary gland would only be drawn years later, after some patients with polyuria and polydipsia were found to have damaged pituitary glands in their autopsies.

In many cases of hormonal excess, pituitary tumours would be found at the autopsies. Drawing a relation between the two, neurosurgeons would attempt to approach the pituitary gland through the cranium, which was only met with devastating consequences as it was associated with high rates of mortality. Neurosurgeons, including Harvey Cushing, would develop new operative techniques such as transsphenoidal surgery. These proved efficient, and the principles of those procedures are still in use to this day.

Exploring Short and Tall Stature in History: Unveiling the Birth of the Human Growth Hormone

The term “little people” typically refers to those with dwarfism. In Germanic mythology, including Norse mythology, a “dwarf” is a supernatural being that typically lives in the mountains. They are known for their handiwork and excellent skills in craftsmanship (see picture 1 and 2).



Picture 1: This picture shows a short dentist with a tall lady.

A Street Scene with a Tall Man Offering Snuff to a Short, Fat Man



A street scene with a tall man offering snuff to a short, fat man. Coloured etching by W.P., 1827. Wellcome Collection. Public Domain Mark. Source: Wellcome Collection

Picture 2: This picture shows a tall man with a short man.

Little people have been mentioned in art and literature since ancient history and portrayed in various ways (see picture 3). During the Renaissance period in Europe, little people were depicted as abnormal creatures and were exploited for comedic and sinister entertainment. Short stature, as well as other physical deformities, were displayed in circuses and theatres for centuries. However, unlike the views during the Renaissance, the Egyptians and Greeks portrayed dwarfs in a more sacral manner. To the Egyptians, the physical distinction was not considered a deformity but rather a divine attribute symbolic of their spiritual beliefs [1].

Throughout history, dwarves were given and received as gifts among rulers. They were treated as accessories to flaunt wealth and high social status. Certain roles were taken on solely by little people. Jester dwarves were primarily used for entertainment, whereas court dwarves often stood next to royals to exaggerate and highlight their power. The typical disdain towards dwarves was emphasised through paintings, where they were illustrated with coldness and ugliness.

A Tall Thin Man Accompanied by a Short Fat Lady Carrying a Fan

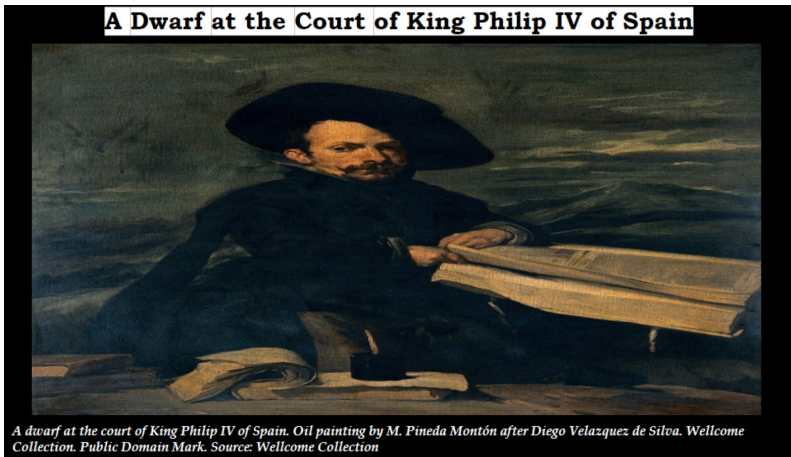


CAPT.ⁿ CONQUEST and his BAGGAGE WAGGON.

London, Printed for Rob^t Sayer, N^o 53 Fleet Street & J. Smith N^o 35 Cheap-side, as the Act directs 15 June 1772

A tall thin man accompanied by a short fat lady carrying a fan. Engraving by J. Goldar, 1772, after S.H. Grimm. Wellcome Collection. Public Domain Mark. Source: Wellcome Collection

Picture 3: This picture shows a tall man with a short fat lady.



Picture 4: This picture shows a dwarf at the court of King Philip IV of Spain.

The Spanish royal court painter Diego Velázquez may have been the first to appreciate the presence of dwarves in court and paint them realistically and with warmth (see picture 4). Velázquez was assigned to paint a portrait of King Phillip IV of Spain. With its realistic touch, the painting impressed the king, and Velázquez was hired as the chamber's painter. His work is still regarded as some of the most impressive artistry in history. One of his well-known paintings, *Las Meninas*, has become a popular topic for historians. The painting is of Princess Margaret Theresa, daughter of King Philip IV and Mariana of Austria. Highlighting their important role in the Spanish court, two dwarves are also seen in *Las Meninas* [1, 2, 3] (see picture 5).

Jan Miense Molenaer, *The Artist Studio* (1631), depicts the emergence of different art by illustrating a group of musicians in the studio of an artist. In the painting, a dwarf and a dog absorb and relish the lively atmosphere [4] (see picture 6).

The shortest adult ever recorded was Chandra Bahadur Dangi, measuring 21.5 inches (54 cm). In 2012, Chandra, who was a Nepali man, was titled "the shortest adult human" in history by Guinness World Records. Chandra passed away in 2015 at the age of 75 [5]. On many occasions and throughout history, the dwarves were pictured alongside the giants (see picture 7).

In 2022, Guinness World Records verified Afshin Esmacil Ghaderzadeh, an Iranian Kurd, as the new world's shortest man alive and the 4th shortest man ever recorded, measuring 65.24 cm (2 ft 1.6 in) [6, 7].

Las Meninas, by Diego Velázquez, from Prado, 1656



Las Meninas, by Diego Velázquez, from Prado in Google Earth.jpg, Public domain, via Wikimedia Commons

Picture 5: This picture shows Las Meninas, by Diego Velázquez.

Jan Miense Molenaer, The Artist's Studio (1631), Showing a Dwarf's Interaction with a Dog through Play



Jan Miense Molenaer, Public domain, via Wikimedia Commons

Picture 6: This picture shows the Artist's Studio, by Jan Miense Molenaer.

A Giant and a Dwarf, London, 1927



A giant and a dwarf, London, 1927. Wellcome Collection. Attribution 4.0 International (CC BY 4.0). Source: Wellcome Collection

Picture 7: This picture shows a giant and a dwarf.

Although the size of dwarves and giants dramatically differs, their fate in humanity has been quite similar (see picture 8 and 9). Like little people, giants have been acknowledged more negatively in ancient times. Most often, they have been represented as intimidating monsters. However, in some settings, gigantism has been used to represent heroes. Although in classical literature Hercules and Prometheus were of average height and size, they have been illustrated as giants in paintings to represent their strength and masculinity [1].

**An Advertisement for the Appearance of the Giant
Andrew and the Little Thomas in London, 1890**

ELEPHANT AND CASTLE THEATRE.
12 NIGHTS ONLY IS
OPEN MONDAY, APRIL 28th, 1890.

MOHAWK MINSTRELS
PROPRIETORS-WILLIAM FRANCIS & HARRY HUNTER
MR ANDREW BANNISTER

THE MOHAWKS GIANT

**AGE 26,
WEIGHT 34st
HEIGHT 6ft 4ⁱⁿ**

GREAT ANDREW LITTLE THOMAS.

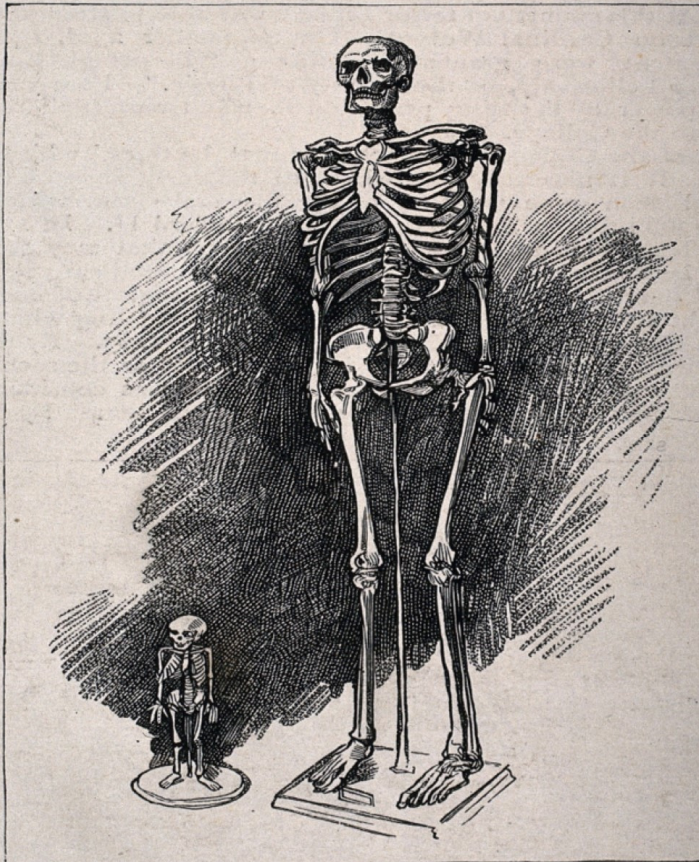
The Marvellous Male Soprano.

LONDON PRINTING & PUBLISHING ALLIANCE LIMITED.
100, NEWINGTON ROAD, S.E.1. (LONDON)

Mohawk Minstrels : Mr. Andrew Bannister, the Mohawks giant... : Little Thomas, the marvellous male soprano / Proprietors, William Francis & Harry Hunter. Public Domain Mark. Source: Wellcome Collection

Picture 8: This picture shows an advertisement for the appearance of a giant and a dwarf.

Skeletons of a Male Giant and a Female Dwarf

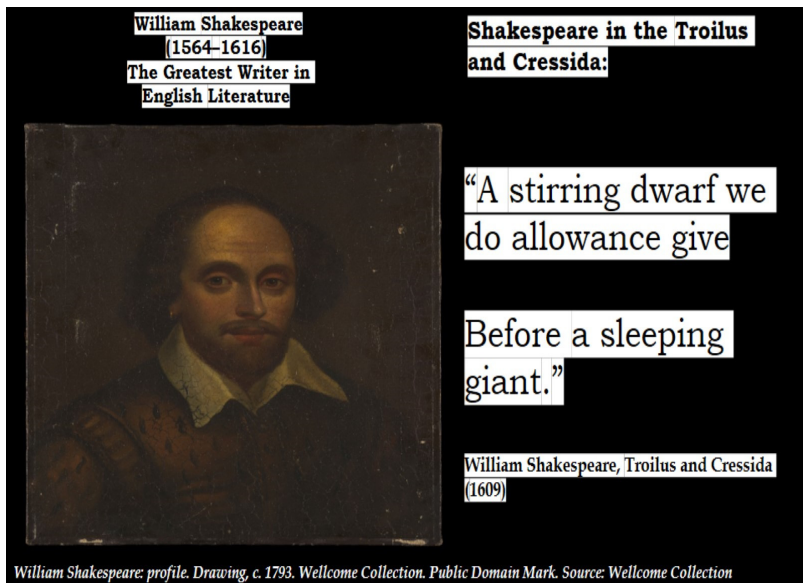


ROYAL COLLEGE OF SURGEONS—SKELETONS OF
MDLLE. CRACHANI, A SICILIAN DWARF, AND
OF O'BRIEN, THE IRISH GIANT

Skeletons of a male giant and a female dwarf, displayed at the Royal College of Surgeons. Process print. Wellcome Collection. Public Domain Mark. Source: Wellcome Collection

Picture 9: This picture shows the skeleton of a male giant and a female dwarf.

In English literature, the dwarves and giants were mentioned many times and in different situations (see pictures 10 and 11). Before scientific advancements, the cause behind the different heights of dwarves and giants was a mystery and an attraction for artists. The discovery of the human growth hormone was a result of investigations of patients with acromegaly. French scientist Pierre Marie described a clinical picture and called it acromegaly back in 1886. Shortly afterward, pituitary tumours were reported to be found in the autopsies of patients fitting this picture. However, the connection between the pituitary gland and growth disorders was initially debatable [8, 9].



Picture 10: This picture shows William Shakespeare. The quotation in this picture is adapted from Shakespeare, William. AZQuotes.com, Wind and Fly LTD, 2023. <https://www.azquotes.com/quote/1040908>. Accessed September 01, 2023.

A Dwarf on the Shoulders of a Giant, in a Rowdy inn. Etching by G. Cruikshank



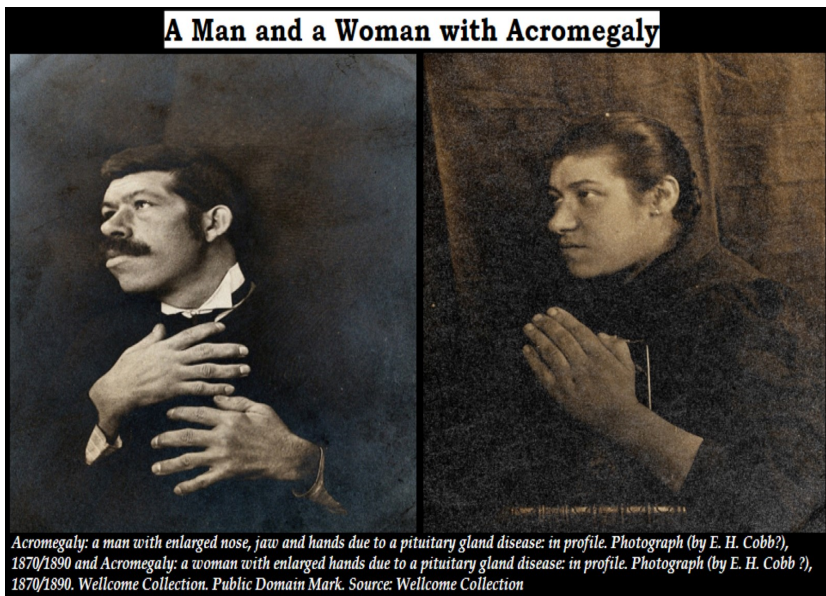
The Stone Kitchen.

“The dwarf sees farther than the giant, when he has the giant's shoulders to mount on.” *Samuel Taylor Coleridge*

A dwarf on the shoulders of a giant, in a rowdy inn. Etching by G. Cruikshank. Wellcome Collection. Public Domain Mark. Source: Wellcome Collection

Picture 11: This picture shows a dwarf on the shoulders of giants. The quotation in this picture is adapted from Coleridge, Samuel Taylor. AZQuotes.com. Wind and Fly LTD, 2023. <https://www.azquotes.com/quote/1043706>. Accessed September 1, 2023.

The name acromegaly is Greek in origin, with ‘Acron’ referring to the extremities and ‘Mega’, meaning enlarged. In the beginning, it was also referred to as Marie’s Malady. Patients who were thought to have “acromegaly” were of tall stature, had abnormally large hands and feet, altered facial structure, and also acquired endocrinological disorders (see picture 12). Although Pierre Marie termed the condition, the clinical presentation of acromegaly was mentioned multiple times throughout history under different names. One of the first descriptions was in 1567, when Johannes Weir reported a “giant female with irregular menses.” This patient used her unusual appearance to exhibit herself to make a living [8, 9, 10].



Picture 12: This picture shows a man and a woman with acromegaly.

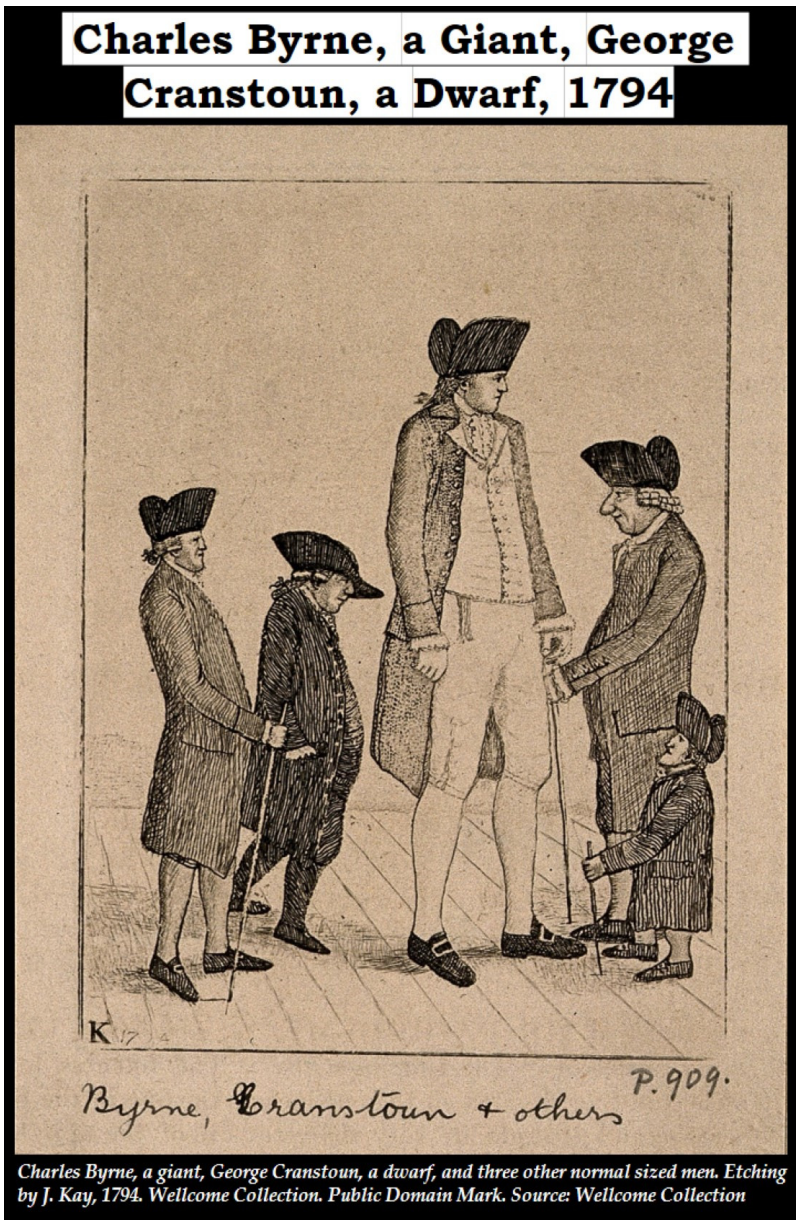
Andrea Vega might have been the first to describe an irregularity in the pituitary glands of these patients. He writes in his report that he had seen a female patient in the church of the public district general hospital in Milan. The patient had acquired the nickname “big face” from the hospital’s staff. She passed away in 1862, at the age of 52, and the autopsy report was performed by Vega. In the absence of a pituitary gland, Vega found a tumour the size of a walnut. This tumour had displaced the optic nerves [9].

Pierre Marie and Jean Charcot had observed two females with acromegaly in Paris. The reports were shared in 1886. One of the cases was a 37-year-old who had stopped menstruating in her mid-twenties and was gradually growing in size. Her face and body were deformed. Her change was so drastic that her family did not recognise her after she returned from the hospital. Pierre reports that this patient had an unquenchable thirst and produced large amounts of urine [9] (see picture 13).



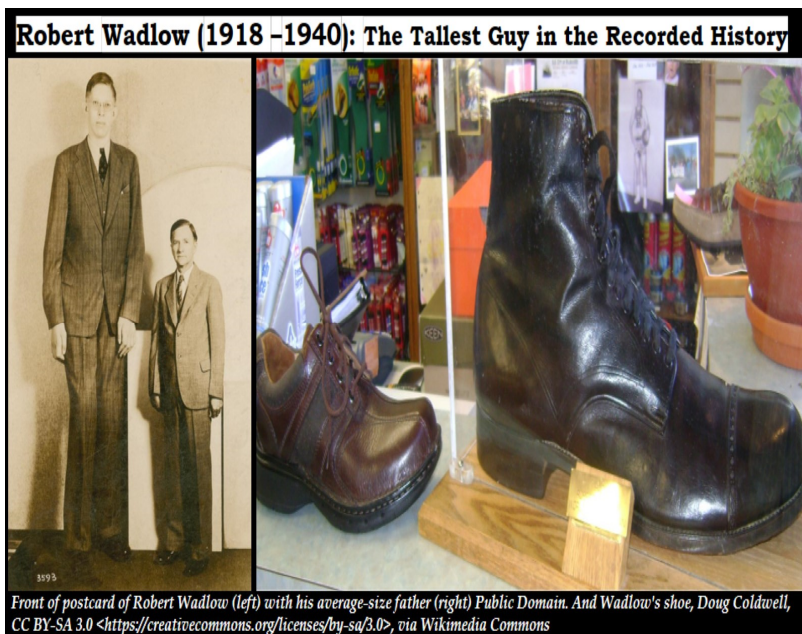
Picture 13: This picture shows Pierre Marie.

A renowned Irish giant and entertainer, Charles Byrne, embodied the description of acromegaly (see picture 14). After his passing, his remains were passed on to John Hunter, a Scottish surgeon. With curiosity and passion, Hunter and neurosurgeon Harvey Cushing performed an autopsy on the giant in 1909 and found an enlarged sella turcica. Charles Byrne's skeleton has been displayed in London's Hunterian Museum since 1799 but was removed in 2023 [9, 11, 12].



Picture 14: This picture shows Irish giant, Charles Byrne.

The tallest person ever recorded in history was Robert Wadlow. The American giant was known as the Alton or Illinois giant and was measured at 8 feet 11 inches (2.72 m). Robert was a member of the Ringling Brothers Circus, where he declined requests to wear ridiculous costumes. He was given a lifetime supply of free shoes from the International Shoe Company for promotion. Unfortunately, due to blistering from the ankle brace he wore to support his legs, Robert developed sepsis and passed away in 1940 at the young age of 22 [13, 14] (see picture 15).



Picture 15: This picture shows Robert Wadlow and his shoes.

Aware that there was a correlation between the pituitary gland and acromegaly, it was still unclear whether the enlarged pituitary was due to acromegaly or vice versa. Many investigations and reports later, an association between acromegaly and hyperfunctioning of the pituitary gland was established [8, 9, 15].

The existence of a 'growth hormone' secreted by the pituitary gland was graspable, but in order to be proven, the hormone needed to be isolated. The first attempt was made in 1922 by Evans and Long, who retrieved bovine anterior pituitary extracts and injected them into rat subjects. This caused