SALVADOR GIL VERNET, A PIONEER IN UROLOGICAL ANATOMY

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Introduction
This chapter intends to present the biography and scientific work of Salvador Gil Vernet (1892-1987). He was an outstanding Spanish anatomist and urologist who made extraordinary discoveries in the field of urological anatomy, in particular with his studies on the topographic anatomy of the male pelvis and perineum and who developed the first urethrocetric model of the prostate’s regional or zonal anatomy. (Fig. 1)

Biography
Salvador Gil Vernet was born in Vandellós, a small town in the province of Tarragona (Spain) on August 10, 1892. As a teenager he showed great passion for the natural sciences and particularly for botany, which he practiced enthusiastically. He dedicated his summer holidays to collecting and classifying a large number of plants. Salvador’s dream at the time was to become a professor at the School of Natural Sciences.

In 1909, at the end of his school years, he moved to Barcelona and entered the School of Medicine at the University of Barcelona, from which he graduated with outstanding grades on June 30, 1915. In 1917 he published a new technique for extradural anesthesia in pelvic surgery.† In 1920 he was appointed assistant professor at the anatomy department. (Fig. 2) Also in 1920, he married Mercedes Vila with whom he had two children: Salvador (1921-1964) and José María (b. 1922); both would become urologists.

† Gil Vernet, S. La anestesia extradural. Nueva técnica. Tipografía S. Vilalta, Barcelona. 1917.
Barcelona, was relieved of all responsibilities. Persecuted by communists, he chose to leave Spain.

Years later he would remember those times:

When, on the evening of August 14 1936, I thought I was saying, ‘Goodbye, forever!’ to my country from the French ship Cortes II, I experienced emotions that were new to me. Suddenly, I had lost everything that a man can possibly lose, saved only honour and life, and these had been saved thanks only to the charity of the diplomats of Nicaragua and France.²

He first lived in Toulouse, France and then in Italy, where he took part in the foundation of the Mediterranean Urology Association. He eventually returned to Barcelona in 1939, once again joining the anatomy department of the University.

In his double professional role as anatomist and urologist, Gil Vernet often noted his findings in the dissection room and in the operating theatre were uncorrelated to the descriptions in the classical topographic anatomy treatises published in the mid-nineteenth century. These contradictions prompted him to an exhaustive and careful study of male urogenital anatomy, which extended over more than forty years. During his long scientific career Gil Vernet delved into his studies with great discipline and effort. As he used to say: “Scientific inspiration does not exist if not accompanied by cerebral sweating”.³ His findings were crucial to comprehending the pathological processes of the prostate and to designing less invasive new surgical techniques for perineal radical prostatectomy.

Thanks to his huge, daunting work during the 1950s and 1960s, the Urological Service of Prof. Gil Vernet would become one of the most prestigious urologic institutes in the world, a venue hosting urologists such as Prof. Adolphe Steg (France), Prof. Ian Thompson (USA), Prof. Ermanno Mingazzini (Italy) or Prof. Willy Gregoir (Belgium) among many others. (Fig. 3) As a result of the

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² Autobiography of sorts
³ Commentary in Salvador Gil Vernet’s obituary, signed by Prof. D. Truano, published in La Vanguardia newspaper, on November 1, 1987.
department’s great international projection, Gil Vernet maintained fruitful exchanges with Prof. Charles B. Huggins by means of frequent correspondence (Fig.4) and being invited as Lecturer to the University of Chicago.

Salvador Gil Vernet retired from his professional activity when he was 75 and dedicated his last years to the cultivation of roses and lemon trees in his house in Castelldefels playa. He passed away in Barcelona on October 24th, 1987.

Awards
In 1948 he became a full member of the Royal Academy of Medicine and Surgery of Barcelona. In 1950 he received an honorary degree from the University of Toulouse. He received the Pedro Virgili Surgery Award from the Spanish Royal Academy of Medicine and the Antoine Portal Award from the National Academy of Medicine of France in 1965.

He was elected president of the Société Internationale d’Urologie (SIU) from 1967 to 1973 and Honorary President of the Spanish Association of Urology in 1967. He was elected Honorary Member of the Societies of Urology of France, Italy, Greece, Mexico and Colombia. He was a visiting lecturer at Columbia University, and at the Universities of Chicago, Buenos Aires, Bogota, Toulouse, Tokyo, Amsterdam, Johannesburg, Mexico and Munich. In 1986 he received, alongside his son José María Gil-Vernet Vila, the Narcís Monturiol Prize awarded by the Government of Catalonia.

Scientific work
In the 1920s Gil Vernet’s research was centered on the study of the topographic anatomy of the male pelvis and perineum, with a specific focus on the bladder, the neural pelvic plexus and the prostate. Following in the steps of German morphologist Hermann Braus, Salvador Gil Vernet considered that it is not enough to determine the “what” and the “how” of an anatomical structure; an answer is needed to the question “what for”. This way he strived to develop a functional urogenital anatomy, which better allowed doctors to understand and explain the physiology of urination, erection and ejaculation. Likewise, Gil Vernet provided new insights into the topographic anatomy of these structures, building bridges with surgery and helping to develop more precise and scientific surgical techniques.

Gil Vernet was an untiring worker in a country, Spain, which after its Civil War was a wasteland for scientific research. Thanks to his effort and perseverance he was able to compensate for the economic hardships of the 1940s and published four books dedicated to the study of urogenital anatomy and pathology as well as over 50 journal publications between 1917 and 1977. Possibly his main work was “Patología Urogenital” (Urogenital Pathology, a three-volume work) focused on the study of the prostate, i.e. embryology, regional anatomy, pathology and surgical techniques. (Fig.5)

Some scholars consider it the most outstanding contribution from Spain to studies in urology. “Morphology and Function of Vesico-Prostato-Urethral Musculature” was another fundamental work dedicated to the study of the topographic and microscopic anatomy of the pelvis and the perineum.

In 1930 he started to apply the histotopographic method, a technique of anatomical study (whole-mount sections) in the uro-anatomy laboratory, (Fig.6) which had been described by the German anatomist Otto Kalischer thirty years earlier.4 With the help of the giant Sartorius-Werke microtome (Fig.7) he obtained frozen sections of the pelvic visceral block from foetal and adult specimens. About 200 preparations were obtained from each specimen, with a thickness of 20 to 50 microns and measuring 12 to 9 centimetres. (Fig.8) Microscopic observation at a magnification of 10x and 100x allowed microscopic dissection of muscle and nerve elements which would otherwise be invisible in macroscopic dissection.

Prof. Gil Vernet annotated the most interesting details in his field books (Fig. 9), which would later be drawn in pencil and Indian ink by the second year students at a scale of 1:7 to 1:15.

December 6, 1961

S. E. Professor S. Gill Vernet
Escuela Profesional de Urología
Facultad de Medicina de Barcelona
Barcelona, Spain

Dear Don Salvador:

Your letter was wonderful! I cherish it. Ultimately it will be translated to my grandchildren.

You are the embodiment of the Catalan genius. You are a second Cajal. One of the greatest honors of my life was to become acquainted with you.

On behalf of the University, I invite you to visit Chicago, either before or after your visit to Puebla. We would like to have you give a lecture to our small group which will be truly appreciated. We would like to have you inspect our work. We implore you to be the guest of the University while you are in Chicago. You will be among friends and admirers from beginning to end.

Yours very respectfully,

Charles Huggins

Figure 4a & b: Letters from Prof. Charles B. Huggins (1961 and 1963).
Figure 5a & b: The first two volumes of “Patología Urogenital”.

Figure 6: The Uro-Anatomy Laboratory. In the foreground, the tube of the coal stove. To the right in the picture, the giant Sartorius-Werke microtome.

Figure 7: Giant Sartorius Werke microtome (ca.1925) used by Gil Vernet. At present it is in the museum of the Faculty of Biology at the University of Barcelona.

Figure 8: Newborn perineum. Transverse histo-topographic section. Van Gieson trichrome stain.
The sensational richness in the details in the drawings of the histotopographical sections was praised by Charles B. Huggins who wrote: "Let the young surgeon study sagittal sections of the pelvis of the human male, for example the beautiful studies of Gil Vernet". Since 2005, a large number of drawings have been collected and restored, amounting to a total of 604 items, which now comprise the Salvador Gil Vernet Collection of Urology Drawings.

The topographic anatomy of the male perineum

His first work, applying the Kalischer's method to the study of the male perineum, was published in 1933. He found that the so-called rectourethral muscle was in fact not a muscle but a complex formed by smooth longitudinal fibres of the external longitudinal layer of the anal canal running to join the fibroconnective tissue of the perineal body and also several dorsocaudal striated fibres of the external urethral sphincter, although these never reached the urethra. (Fig.11)

Gil Vernet considered the term "rectourethralis muscle" a misnomer, and in later studies he coined the term "rectourethralis system". Currently it is known as the "rectourethralis complex". In 1944 he demonstrated that the superficial transverse muscle is made up of fibres that anastomose from the anus's external sphincter with fibres of the bulbospongiosus muscle and never insert into the ischiopubic rami. (Fig. 12) He also studied in great detail the male perineal body and the various muscle and fibroconjunctive elements that make it up.

The external urethral sphincter

In 1836 the German anatomist Johaness Müller described the urethral sphincter as a vertical structure. However, thirty years
Figure 10: Drawing corresponding to the section in Figure 8. Indian ink on paper, 45 x 28 cm. Artist: L. Roca, 1943.

Figure 11: Rectourethralis system (arrowheads). Membranous urethra (MU), external urethral sphincter (arrows), bulbourethral glands (BG), corpus cavernosum (CC) and rectum (R). Male newborn Transverse section. Haematoxilin-eosin stain. Indian ink on paper, 83 x 49 cm. Artist: L. Sala, ca.1945.
later, his disciple Friedrich Henle\textsuperscript{11} considered that the sphincter was actually divided into a proximal portion called “sphincter vesicae externus” and a distal portion that was called deep transverse perinei muscle; an error that was included in texts of atlases and anatomy books until the end of the twentieth century.

Gil Vernet was concerned with improving urinary incontinence after radical surgery of the prostate so he set to study the urethral sphincter extensively. What he observed in his dissections and perineal radical prostatectomy did not match the descriptions offered in textbooks. In the 1940s - for the first time in the twentieth century - Gil Vernet described the sphincter as a tubular structure, vertically arranged and consisting of two layers, i.e. an internal layer formed of circularly - and longitudinally - arranged smooth muscle and an external layer of circular striated fibres which were divided into three areas: cranial, medial and caudal. (Fig.13)

He also demonstrated that the deep transverse muscle of the perineum was a non-entity and that the structure surrounding the bulbourethral glands consists of the dorsocaudal fibres of the urethral sphincter that do not insert into the ischiopubic branches.\textsuperscript{8,12}

The urethral crest and the posterior prostato-urethral muscular bundle

In 1953 Gil Vernet described a group of dorsal and longitudinal smooth urethral musculature which he referred to as the posterior prostato-urethral muscular bundle, (Fig.14) and which forms the relief of the mucosal fold.\textsuperscript{12} This muscular bundle originates below the ejaculatory ducts at the lower pole of the colliculus seminalis, and runs dorsally and downwards ending into the penile bulb. The function of this muscle is to shorten and dilate the infra-collicular urethra during ejaculation.

Topographic anatomy of the bladder

Always guided by a clear functional purpose, Gil Vernet

Figure 13: External urethral sphincter (arrowheads). Prostate (P), rectum (R), levator ani muscle, membranous urethra (U), ischiopubic rami (IR), ischiocavernosus muscle (IC), penile bulb (PB), and bulbospongiosus muscle (BS). 6-month male foetus. Coronal section. Haematoxilin-eosin stain. Indian ink on paper. 71 x 65 cm. Artist: J. Costa, 1944.

Figure 14: Posterior prostato-urethral muscular bundle (arrows). Coronal section. Haematoxilin-eosin stain. Indian ink on paper. Unknown artist, ca. 1953.
tried to unravel how anastomoses are formed between the various ganglionic areas during embryonic development. Faced with the enormous complexity of this endeavour, he sought advice from Santiago Ramón y Cajal, whom he had met in 1920 as chairman of the Opposition Committee for the chair of Anatomy. From then on, the men maintained correspondence. (Fig.17)

From 1940 he began to study embryology and neuroanatomy of the pelvic plexus and, specifically, the innervation of the bladder, seminal vesicles, prostate and external urethral sphincter.8,17 He showed that the vertical extension of the pelvic plexus follows the posterolateral border of the prostate, forming the neurovascular bundles. In the descending part, nerve branches split off that penetrate the prostate gland, membranous urethra and external urethral sphincter, with the terminal branches forming the nerves of the corpus spongiosum and the cavernous nerves. (Fig.18)

He also described a ventral prolongation of the pelvic plexus that forms what he called the anterolateral and anteromedial neurovascular pedicles, which run downwards, giving off branches to the membranous urethra. He wrote:

“At every one of the four corners of the rectangle that makes up the prostatic cell, a neurovascular bundle is observed, and those are the bundles which carry the vessels and nerves intended for innervation and irrigation of the prostate, membranous urethra and the cavernous nerves, enabling erection.”

This description of the prostate neurovascular bundles was corroborated by the superb work of Patrick Walsh, which served as the anatomical basis for the development of nerve sparing radical prostatectomy.18,19 The arrangement of the membranous urethra

Pelvic plexus neuroanatomy

Since his youth Salvador Gil Vernet took a great interest in the abdominopelvic vegetative nervous system. Thus in 1918, he was the first to describe the inferior mesenteric ganglion in men.15 In 1926 he published “El Sistema nervioso órgano-vegetativo. Contribución a su estudio anatómico y embriológico”,16 where he

16 Gil Vernet, S. El Sistema nervioso órgano-vegetativo. Contribución a su estudio anatómico y embriológico. Imprenta Badía, Barcelona, 1926.
Figure 15: Anterior face of the bladder and space of Retzius. Adult male. Transverse precervical arc (arrowheads). Mixed media on paper. Artist: F. Nuñez ca. 1951.

Figure 16: Posterior face of the bladder. Adult male. Posterior longitudinal fascia of the detrusor (arrowheads). Seminal vesicles (SV) and prostate (P). Adult male. Mixed media on paper, 23 x 21 cm. Artist: F. Nuñez, ca. 1945.
INSTITUTO CAJAL

Madrid 5 de Octubre de 1925.

Amigo Gil Vernet:
Propone V. un tema difícil y sobre el cual solo conjurarías cabe esparcer.

Desde luego anastomosis verdaderas no existen, quiere decir unidas substanciales entre axones de diversas procedencia.

Pero si no hay continuidad, existen como se sabe colaboraciones de axones de origen diferente en la constitución de un nervio o filamento nervioso anastomosado (plexus braquial, sacroileígeno etc.). La hipótesis que yo formule hace tiempo del leucocitoplasmo, se dice que los cilindros ejes que llevan paródida camino se astraen para formar cordones mícticos, puede todavía defendernos sobrestando desde el punto de vista neurofisiológico formación de las raíces nerviosas, pero requiere 1) Mas poderían entrar en juego otras influencias y medios que por el pronto no se me ocurre puntualizar. En estos últimos años están muy de moda para explicar la neurotización del cable periférico de los nervios corticofugos, las diferencias de potencial eléctrico entre los axones centrales y las vainas de Schwann del cable periférico. Pero esto constituye una hipótesis que exige demostración.

Sabe yo lo sé veras su compañero y amigo.

Santiago Ramón y Cajal

Figure 17: Letter from Santiago Ramón y Cajal to Salvador Gil Vernet. 1925.

Figure 18: Left neural pelvic plexus. Adult male. Mixed media on paper, 28 x 31 cm. Artist: F. Nuñez, 1944.
and inferior branches of the pelvic plexus along the ventral surface of the prostate was also corroborated many years later.\textsuperscript{20}

In his studies on the membranous urethra and the external urethral sphincter, he described the presence of microscopic periurethral nerve ganglia and tiny nerve branches, a continuation of the pelvic plexus, which penetrate the mass of the external urethral sphincter. (Fig. 19) He thus assumed that autonomous nerves innervated the striated fibres of the urethral sphincter, contradicting the classical conception of the external urethral sphincter, only receiving somatic innervation through the internal pudendal nerve.

In addition, he assumed that some fibres of the internal pudendal nerve, following an intrapelvic pathway, joined the hypogastric ganglion very close to the entry of the pelvic nerves and innervated the striated urethral sphincter through the most caudal efferent branches of the pelvic plexus.\textsuperscript{12} More than 50 years later, several authors confirmed in their publications this double innervation, i.e. somatic and autonomic, of the external urethral sphincter.\textsuperscript{21, 22, 23, 24}

In his works on surgical technique, mainly those focusing on radical perineal prostatectomy, he highlighted the significant impact of preserving the nerves of the pelvic plexus on the incidence of postoperative urinary incontinence.\textsuperscript{6}

**Regional anatomy of the prostate**

In 1953, Gil Vernet described the first regional anatomical model of the prostate gland. He clearly demonstrated that the prostate is not a homogeneous gland and that it consists of three regions: the cranial, the caudal and the intermediate glands.\textsuperscript{10, 25} He wrote:


“...accepting the principle of duality of the prostate gland as valid, we believe that a detailed analysis of these complex problems will not unequivocally support the conclusive division between the cranial gland and the caudal gland. It is necessary to insert a portion between both poles, which we shall call the intermediate gland, establishing a smooth transition between the cranial and caudal portions.”

This model was urethrocentric, with areas defined according to the location of their collecting ducts opening into the urethra (Fig. 20) and was later used by McNeal, with very small variations, as the foundation of his zonal anatomy model.26, 27, 28 The cranial gland is formed by intrasphincteric glands, located within the internal vesical sphincter (Albarran’s periurethral glands), and two subsphincteric lateral lobes, which correspond to the transition zone in McNeal’s model.

The caudal gland is formed by the posterolateral and apical (dorsal and ventral) surfaces of the prostate, the collecting ducts of which open distally beyond colliculus seminalis, on both sides of the urethral crest. This region is identical to the area described as the peripheral gland in McNeal’s model, although this author ignored the glands located on the ventral apical surfaces of the gland, in what he called the anterior fibromuscular stroma. The collecting ducts of the intermediate gland drain into the colliculus seminalis at the opening of the ejaculatory ducts. The glandular acini are located dorsolaterally to the pathway of the ejaculatory ducts forming the craniodorsal surface of the prostate. This intermediate gland is identical to McNeal’s central zone.

In Gil Vernet’s embryological studies the caudal gland is induced by the urogenital sinus mesenchyma. The cranial and intermediate glands are induced by an area of mesenchyma, which consists of the fusion of the Wolffian and urogenital sinus mesenchyma.

Gil Vernet observed that benign hyperplasia develops in the cranial gland and that carcinoma develops in the caudal gland. Prof. Charles B. Huggins cited this major work: “The Gil Vernet Phenomenon wherein the human prostate is separated into two physiologically and oncologically different divisions, is of permanent value. It is a wonderful discovery.”

Conclusions

Salvador Gil Vernet combined a keen interest in morphological sciences from an early age, a passion for urology and an enormous capacity for working. This allowed him to spend endless hours behind the microscope and in the dissecting room. His first observations concerning the urological anatomy of both embryo and adult did not correspond with the concepts described in traditional works. This led him to question whether past thinking was, in fact, true, and to try and find ab initio, based on his own experience, what the true anatomy of the pelvis and the perineum really was.

Through the histotopographic technique, he managed to achieve a perfect microscopic dissection, which allowed him to unravel the innermost secrets of topographic anatomy, and apply this knowledge as an urologist to attain better understanding of urogenital physiology and pathology, and develop more effective surgical techniques, ultimately opening the doors to scientific urology. In his own words:

“Precise, almost mathematical, knowledge of anatomy is a highly fertile source of surgical applications, suggesting new techniques and helping to perfect and simplify existing surgical methods, making them less mutilating and more benign and, in short, raising surgery to the rank of true science.”

After Salvador Gil Vernet’s retirement, his son, Jose María Gil-Vernet Vila, professor of urology and a worthy disciple of his father, took over and upheld the urology department’s prestigious reputation, becoming a pioneer in kidney and pancreas transplants in Spain and in the invention and development of new surgical techniques in urology, but that’s quite another story.