

## REVIEW

# Prostate cancer: anatomical and surgical considerations

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### Keywords

### Introduction

Sometimes the past has to be recalled for the present to be vindicated; this is the case with cancer of the prostate (CaP). I shall comment and enlarge upon some aspects of this pathology, which has reawakened the interest of European urologists after 30 years. The publications by Walsh *et al.*, e.g. [1], on radical prostatectomy using the nerve-sparing procedure, have indeed had an influence, and although both the anatomical descriptions and the idea of sparing these nerve formations are not original to these authors and, oncologically speaking, are debatable, their merit in promoting radical prostatectomy should be acknowledged.

Today, as in the past, there are two therapeutic strategies for CaP; one aims to cure the localized process, the other to control the disseminated disease. The therapeutic option for curing the localized disease is still radical prostatectomy, although radiotherapy is also used in some patients with localized CaP.

### Historic events

There are four milestones in the 90-year history of research into CaP; in 1905, when Young, the undisputed master of prostatoperineal surgery, ushered in the age of radical surgery via the perineum [2]; in 1941, with Huggins and Hodges [3] and their important discovery of endocrine therapy; in 1944, with the research of S. Gil Vernet [4] into the origin and development of CaP and his contribution to the knowledge of prostate pathology and surgery, as well as his original description of the musculature and innervation of the pelvic urogenital

block; and finally, in 1945, with the retropubic approach for radical prostate surgery by Millin and Macalister [5]. Since then, nothing new has appeared under the sun; there have been no new basic or innovative concepts and no new anatomical descriptions.

Between 1950 and 1980, surgery for CaP in Europe went through its 'darkest hour'. In 1956, in his magnificent *Traité de technique chirurgicale*, Fey wrote about prostatectomy for cancer: 'This ideal operation is almost unperformable, and has been almost completely abandoned in France, despite various attempts, despite the example of the Americans, with Young, and of the Spaniards, with Salvador Gil Vernet, who still perform it with excellent results.' [6]. This progressive decrease in surgical aggressiveness towards prostate cancer was due to several factors: (i) the excessive enthusiasm aroused by oestrogen therapy; (ii) the fact that very few patients, only 5–10% of cases, presented with limited neoplasias to the surgeon; (iii) the complications inherent in the operation (fistulae, incontinence, stenosis, impotence); (iv) technical difficulties, i.e. the depth of the operative field, haemorrhage of Santorini's plexus and, in particular, the anastomosis of the membranous urethra to the bladder.

Although many years have elapsed, the main strategies to follow in CaP are still manual surgical exploration, hormone therapy and radical surgery. So today, in 1996, if an editorial were to be written on this subject, it would not differ basically from the one by the Nobel laureate Charles Huggins, that appeared in 1969 [7]. He proposed three indications for radical prostatectomy in which the operation could be life-saving: (i) early cancer; (ii) late cancer made operable by endocrine means; and (iii) recurrent prostate cancer after hormonal control.

To avoid two major complications of radical prostatectomy, rectal fistulae and incontinence of urine, Huggins advised young surgeons to study sagittal sections of the pelvis of the human male — 'for example, the beautiful studies of Gil Vernet'. He also stated: 'Radical prostatectomy is for the technician who loves technique, who

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This article is dedicated to the memory of Salvador Gil Vernet, Professor of Anatomy and Urology of the University of Barcelona, Spain (1892–1987), who devoted most of his scientific life to research into the normal and pathological prostate gland. His investigations merited the Presidency of the International Urologic Society from 1967 to 1973.



adores a quiet operative seance where things move along with perfect communion and trust between the chief and the team... — it is a live-saving operation. Radical prostatectomy is for the surgeon who cares. For cancer is safest when completely removed and preserved in pickle.'

### Anatomo-pathological concepts

Today, the division of the prostate gland proposed by S. Gil Vernet in 1953 is universally accepted; it establishes three major segments, the cranial gland, the caudal gland and the intermediate and transitional gland (Fig. 1) [8,9]. Universally accepted also is that the cancer is pathogenically independent of adenoma, because it has a different topographical and embryological origin. Adenoma originates and develops in the cranial prostate, whereas cancer arises in the caudal prostate. This difference is explained by the distinct embryological origin of the two pathologies. According to S. Gil Vernet, the cranial prostate, bladder neck and trigone originate in the mesoderm, while the caudal prostate originates in

the ectoderm. These two regions react in different ways to physiological stimuli [10,11].

Cancer may originate in a normal prostate and it then constitutes the so-called primary cancer of the prostate, of exceptional presentation, but in most cases the cancer coexists with a pre-existing benign hyperplasia. The cancer arises in the prostate gland, properly speaking, totally separate from the co-existing benign hyperplasia; the opposite never occurs.

In some cases, the cancerous focus is single, but most frequently several independent foci are observed, the location of which varies. They may originate anywhere in the gland, but mostly appear in the superficial peripheral portion adjacent to the prostatic capsule, either in the posterior or lateral lobules. Another favourite site is the internal aspect of the lateral lobule adjacent to the adenoma, that is, in the intermediate or transitional prostate (Fig. 2).

These multifocal tumours are independent of each other, possibly appearing asynchronously, and may have different structures, with zones at different stages, and independent phases of latency and growth. Furthermore, they may spread in different ways and metastasize to different sites and at different times.

In 1944, S. Gil Vernet introduced various modifications in the light of new anatomical knowledge, describing the neurovascular formations that run along the lateral portions of the prostate; these formations emanate from the hypogastric plexus and are responsible for the innervation of the external sphincter of the urethra and also contain the erector nerves [4]. In 1953, the same author published his research into the connective stroma, vessels and nerves of the prostatic region, reporting: 'In radical subcapsular prostatectomy, when I have respected the nerve columns situated on the

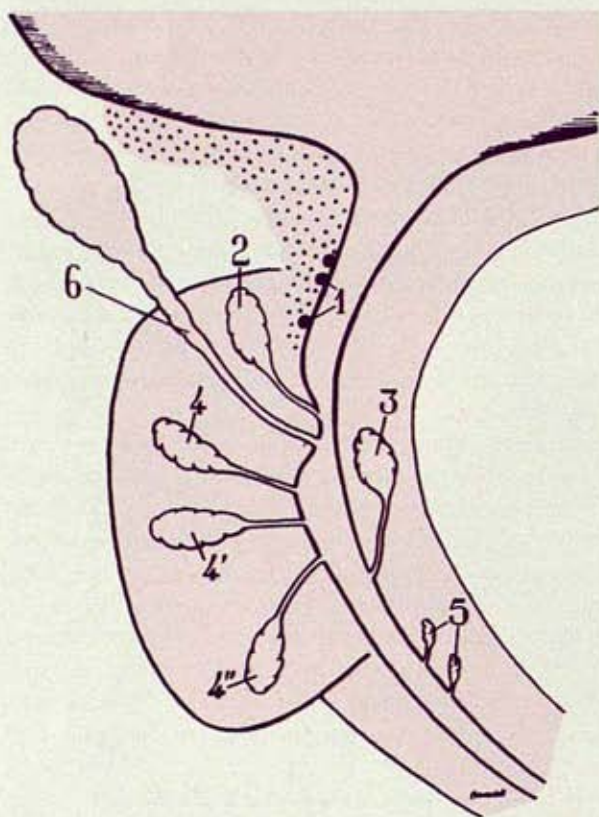


Fig. 1. Diagram of a sagittal section of the prostate. 1, Intrasphincteric submucous glands. 2, Mid-portion of the cranial gland. 3, Anterior lobule of the caudal gland. 4', Superior duct. 4'', Inferior duct of the caudal gland. 5, Littre's glands. 6, Ejaculatory duct (from [9]).

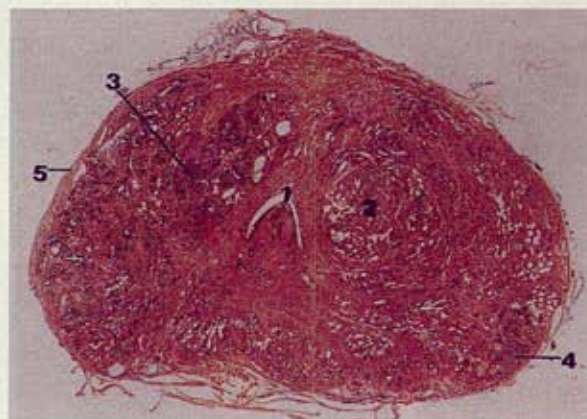


Fig. 2. 1, Urethral duct. 2, Undamaged adenoma. 3, Cancerous focus on the inner aspect of the lateral lobule, spreading to the small adenoma. 4, Cancerous focus on the posterolateral edge of the gland on a peripheral site adjacent to the capsule. 5, Prostatic capsule or fibromuscular covering (from [4]).



posterolateral edge of the prostate, there is no urinary incontinence, whereas with radical extracapsular (extra-aponeurotic) prostatectomy, that is the extirpation of the prostate with its lodge, the walls of which contain the nerve formations, temporary or permanent incontinence is the rule.' [10].

Because there is some confusion about what is meant by prostatic capsule and prostatic lodge, and because the terms intracapsular or extracapsular, and intra- or extra-aponeurotic radical prostatectomy are vague, a definition must be established, from both the anatomical and surgical perspective. The entire prostate is enveloped by a covering 0.5 mm thick, except where the gland joins the bladder, where it increases to a thickness of 2 mm. This covering is half smooth muscle fibre and half fibrous tissue and is, strictly speaking, the prostatic capsule or capsula vera, a dense fibromuscular casing that completely surrounds the prostate except at the level of the anterior aspect (Fig. 2).

Outside the fibromuscular casing that surrounds the periphery of the prostatic gland there is another much thicker fibrous covering which envelops it completely and constitutes the so-called prostatic lodge, formed by an adventitious fibrovascular covering because it contains within its walls the vascular and nerve columns from the hypogastric plexus. Between the prostatic lodge and the capsule is a cleavage which makes it possible, by blunt dissection, to isolate or remove the prostate, leaving part of its lodge (Fig. 3).

This is what surgeons did when they used the perineal route and performed the total subcapsular or intra-aponeurotic prostatectomy now popularized by Walsh *et al.* [1], to distinguish it from total extracapsular or extra-aponeurotic prostatectomy, which is more radical and also includes removal of the prostatic lodge together with the vessels and nerves contained within. S. Gil Vernet had stated in 1953: 'if these are preserved, urinary continence and erection are ensured; otherwise, incontinence is common, though temporary, and erectile impotence persists.' [10].

In 1972, Jewett *et al.* [12] drew attention to the risk of resecting too close to the tumour, with the possibility of leaving tumoral tissue behind and therefore of performing an incomplete operation. A way of performing a more complete removal of the neoplasia was thus required and, along these lines, extracapsular (extra-aponeurotic) radical prostatectomy was described [12,13].

A knowledge of the routes of dissemination of CaP is of great interest in surgery. From the caudal prostate, the focus of neoplasia spreads centripetally and centrifugally, like an oil stain. Centripetal dissemination follows the adenomatous route and contamination occurs at the lower end of the adenoma, which acts as a conductor

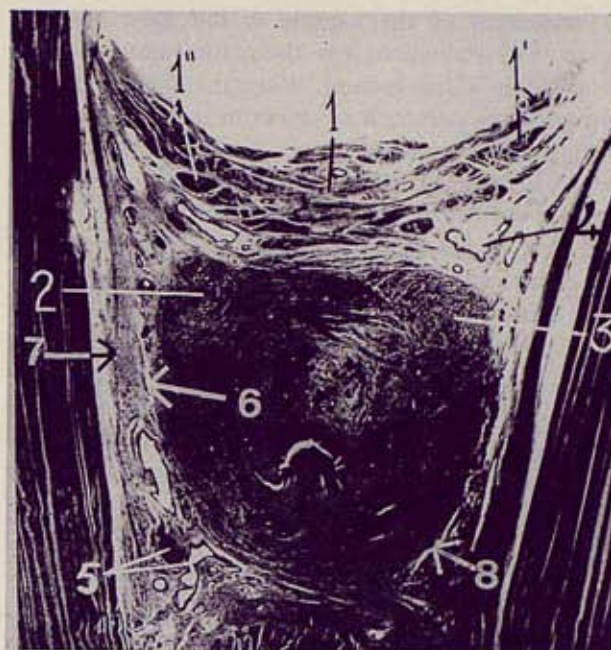


Fig. 3. Frontal section of the prostate. 1, 1' and 1'', Muscle fibres of the retromysophical vesico-urethral system. 2, and 3, Lateral portions of the external sphincter. 4, Anterolateral neurovascular bundle. 5, Posterolateral neurovascular bundle. 6, Prostatic capsule. 7, Prostatic cell or lodge. 8, Cleavage (from [9]).

for the neoplastic elements and carries them to the region of the bladder neck. Centrifugal dissemination is the most important and may occur by three routes; the lymphatics, the perineural spaces and the venous route through Santorini's venous plexus. The prostate lymphatics drain into the periprostatic subcapsular network, from which three groups of ducts originate; the ascending, from the cranial gland, running to the external iliac nodes; the lateral, running to the hypogastric nodes; and the posterior, from the caudal gland, running towards the lateral and subaortic sacral nodes of the promontory. When neoplastic offshoots leave the prostatic capsule through the lymphatics and the perineural spaces, they follow the cellular interstices of the lateral prostatic neurovascular columns that pass through the space between the capsule proper and the wall of the lodge, and from there they may follow the ascending (genital) route or the descending route, when the tumour lies at the apex of the prostate, invading the external sphincter, Santorini's plexus and other neighbouring structures.

The venous path is one of the principal routes of spread; invasion of the periprostatic venous plexus occurs early. The pelvic venous circulation possesses some special anatomical and haemodynamic features, being formed mostly by veins devoid of valves, and therefore constitutes an inert system of blood lakes closely linked to the low-pressure veins of the skeleton.



Penetration of the capsule is the most common route of dissemination; it is 'the natural history' in the propagation of this tumour. When the CaP reaches the intraprostatic nerves, it advances in their sheaths and, through the perineural spaces, penetrates the capsula vera. The dissemination of CaP through the perineural space is well known and is observed in 85% of all cases, including small tumours. For many years the 'perineural lymphatic' spread of CaP has been accepted, but it has now been shown clearly that there are no lymphatics in the perineural spaces; there is only interstitial plasma and collagen fibres (Figs 4, 5 and 6).

Recently, on examining surgical specimens, Villiers *et al.* [14] found that tumoral penetration of the capsule takes place in specific areas that coincide with the points

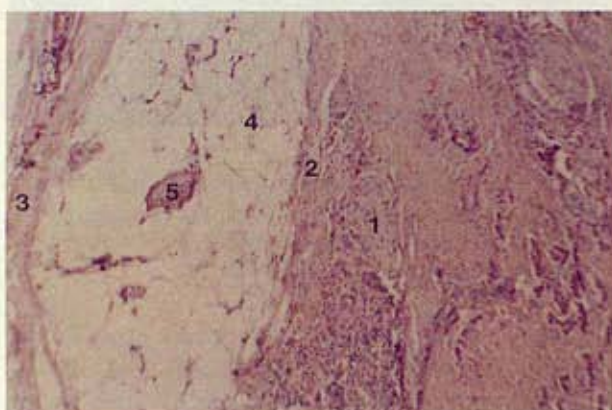


Fig. 4. Tumoral invasion of the capsule through the perineural spaces. 1, Nerves surrounded by neoplastic cells. 2, Prostatic capsule (dense fibrous covering). 3, Wall of the prostatic cell (adventitious fibrovascular covering). 4, Cleavage (pericapsular adipose tissue). 5, Nerve between capsule and prostatic cell wall with endoneurial infiltration.

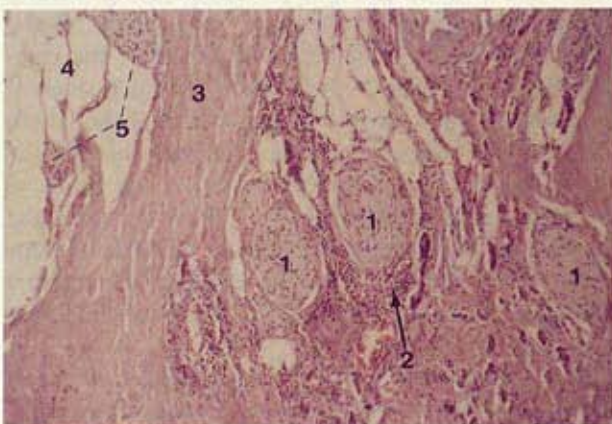


Fig. 5. Tangential section of the prostatic capsule. 1, Nerves penetrating towards the capsule. 2, Infiltration of the perineural space. 3, Collagen fibres of the prostatic capsule stained red with eosin. 4, Adipocytes and loose connective tissue. 5, Nerves in the space between capsule and cell.



Fig. 6. 1, Bundle of nerve fibres. 2, Epineurium. 3, Perineurium. 4, Perineural space. 5, Tumour cells inside the perineural space.

of entry of the prostatic nerves. They reported that the capsule was penetrated in half of their patients with stage B cancer and found that in half of these dissemination had occurred through the perineural spaces.

After lying dormant for several years, the controversy surrounding the innervation of the external sphincter is, with the resurgence of radical prostatectomy, once again a topical issue because of the problem of urinary incontinence in operated patients, just as it had been in the past.

As a result of his investigations, S. Gil Vernet presented a new scheme of innervation, in which the pudendal nerve plays no part in the innervation of the membranous urethra and its external sphincter. The bladder, the bladder neck and the membranous urethra, with the external sphincter, are fully innervated by the hypogastric plexus, to the exclusion of the pudendal nerve. The author made special reference to the fact that: 'As well as parasympathetic fibres, the erector nerves contain somatic fibres, probably destined for the external sphincter muscle.' [15] (Figs 7 and 8).

Many authors have supported S. Gil Vernet's hypothesis [9,10] that the striated sphincter does not receive its innervation through the pudendal nerve, but from the hypogastric plexus, and that through it, some somatic fibres from the sacral core of the pudendal reach the external sphincter uninterrupted in the neurones of the hypogastric plexus [16-19]. Similar work is that by Koyanagui *et al.* who showed that after radical prostatectomy, the urethral sphincter mechanism is more influenced by the autonomic system from the hypogastric plexus than by the somatic system [20].

S. Gil Vernet's findings have been confirmed by recent work on the ontogeny of the hypogastric plexus and its relationship with the genitourinary organs. Arango-Toro and Domenech-Mateu [21], using three human embryos of 19, 25 and 30 mm in length VC, described a nerve branch originating from the main trunk of the internal



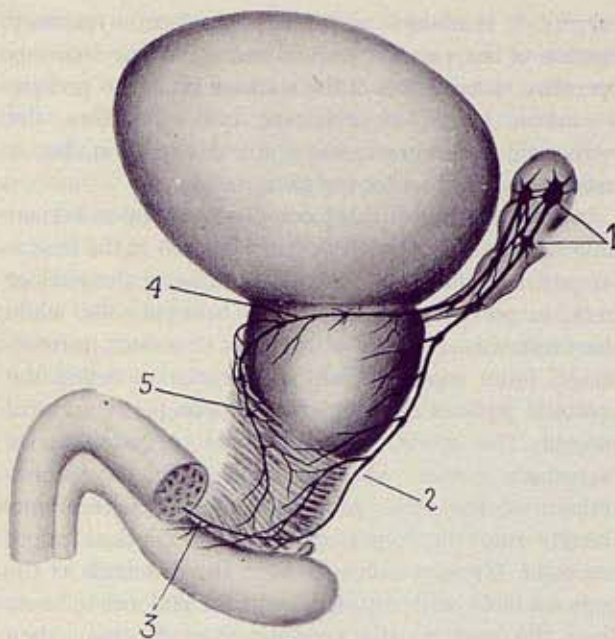


Fig. 7. 1. Hypogastric plexus. 2. Posterior prolongation of the hypogastric plexus. 3. Nerves to the corpus cavernosum and the corpus spongiosum. 4. Anterior prolongation of the hypogastric plexus. 5. Nerve branch to the anterolateral portion of the membranous urethra (from [15]).

pudendal nerve, crossing medially through the mesenchyma and joining the lower half of the hypogastric ganglion. This represents an anastomosis between the somatic and the autonomic systems.

As a result of clinical observations of urinary incontinence following radical prostate surgery, authors in the English-speaking world are beginning to question Learmont's classical scheme, according to which the external sphincter is innervated exclusively by the pudendal nerve, and to acknowledge that the innervation of the external sphincter has not been fully elucidated, as both the autonomic and the somatic innervation of the sphincter area are damaged in this surgery [22].

What is clear, from the standpoint of surgical anatomy, is that in the course of radical prostatectomy, whether this be retrograde or anterograde, the internal pudendal nerve and its branches cannot be damaged, as both the deep and the superficial perineal nerve pass beneath the urogenital diaphragm, while the prostate lies above it and the membranous urethra is within the walls of the diaphragm [23].

Therefore, it seems clear that the recent anatomical findings, the clinical observations of the different results from the nerve-sparing and non-nerve-sparing surgery, as well as elementary anatomical and surgical considerations, support the thesis of S. Gil Vernet that the efferent nerves of the hypogastric plexus contain, in addition to parasympathetic fibres, somatic fibres from the medul-

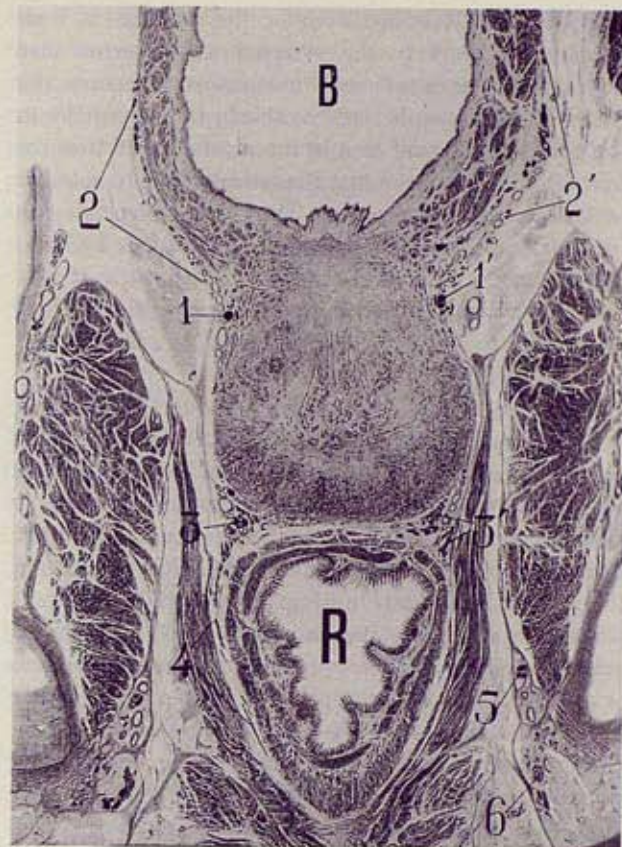


Fig. 8. B, Bladder. R, Rectum. 1, and 1', Anterolateral neurovascular bundles. 2, and 2', Nerves of the bladder. 3, and 3', Posterolateral neurovascular bundles, inferior prolongation of the hypogastric plexus. 4, Rectal nerve fibres. 5, and 6, Bifurcations of the pudendal nerve (from [9]).

lary nucleus of the pudendal (Onuf's nucleus), the destination of which is the striated muscle of the external sphincter [24].

### Surgical considerations

The surgical strategy for CaP should necessarily follow two basic principles of oncological surgery: early ligation of the pedicle before any manipulation, to prevent dissemination of the neoplasia, and resection of the organ together with its covering, with a surgical safety-margin, a concept which is accepted universally.

Prior hormone therapy is useful when given for voluminous adenomas and makes the operation less difficult, but it must be emphasized that radial propagation of the tumour may go unnoticed by the surgeon. For this reason, in patients previously given endocrine therapy and undergoing radical prostatectomy, the obligatory per-operative histological monitoring of the tumour margins should be more exhaustive than in patients who have not received hormone treatment.



In practice, it is common for the surgeon to limit lymphadenectomy to the external and internal iliac nodes, which is insufficient and incorrect because the cancer is known to become established preferentially in the peripheral caudal area of the prostate, and that the ducts in this area drain into the lateral sacral lymphatics and those of the promontory. Thus, a 'complete' staging lymphadenectomy should include these nodes and also a small one which lies against the hypogastric plexus. Frozen sections of all these ganglia should be examined and if they prove to be negative, then radical prostatectomy is performed.

The perineal route for radical prostatectomy (Young 1905, Lowsley 1940, Belt 1942, S. Gil Vernet 1944, cited in [13]) is the most anatomical and the first in which the nerve-sparing technique was used. This is suitable for very obese patients, in whom the other approaches are cumbersome for the surgeon; in addition it is less traumatic and involves less bleeding. The main drawbacks of the perineal approach are that lymphadenectomy cannot be performed simultaneously, the route is so narrow that the appropriate surgical margin cannot be obtained and, because resection is carried out within the prostatic lodge, the technique is not guaranteed to be sufficiently radical.

The retropubic route [5,13,25,26] is familiar to the surgeon and the anatomy of this pelvic space is less complex than that of the perineum. It also provides a wide field for surgical manoeuvre; it preserves the urogenital diaphragm and the vascular and nerve formations therein; it permits simultaneous complete lymphadenectomy and provides easy access to the neck of the bladder and the lateral prostatic pedicles. It should also be stressed that the entire resection is performed under direct vision. The greatest disadvantage of this route lies in anastomosing the urethra and bladder deep within the pelvic cavity, which must be precise, as it is crucial for the patient's future micturitional dynamics.

With the retropubic route, prostatovesiculectomy may be retrograde or anterograde. The bottom-to-top resection [5, 25], after sectioning the puboprostatic ligaments, begins with ligation of Santorini's plexus using Chute's manoeuvre [27], whereby a clamp (16 mm thick) is passed at right-angles between the anterior aspect of the membranous urethra (duly catheterized) and the posterior aspect of the retrosymphysial vesico-urethral system. The ligation cannot always include the entire venous complex and consequently the blood-loss following sectioning of the urethra cannot always be prevented, which makes it more difficult to dissect and visualize the anatomical planes of the prostate and often requires transfusion of the patient. After release of the vesicles and section of the bladder neck, the resection concludes with ligation of the prostatic pedicles. In oncological

surgery it is always advisable to perform a primary ligation of the vascular pedicle and avoid any vigorous operative compression of the tumoral organ, to prevent a possible spread of metastatic cells. Therefore, the retrograde technique is easier for the surgeon, but it may not be the best for the patient.

In 1959, Campbell [26] described the top-to-bottom anterograde technique, with early ligation of the vascular pedicles immediately after sectioning of the bladder neck, to prevent dissemination of tumoral cells, while the urethra is sectioned at the end, to reduce haemorrhage. From top-to-bottom, it is easier to define the prostatic pedicles and achieve the appropriate surgical margin. The operation is performed in conditions of 'neoplastic asepsis' when the main route of dissemination, i.e. the large genito-vesical vein which runs directly into the hypogastric vein, is blocked before resection. My approach is to start the dissection of the tumoral block with an incision in the endopelvic fascia from the apex to the prostatovesical junction, then section the puboprostatic ligaments and ligate Santorini's plexus (Chute's manoeuvre), but without cutting it, and then to proceed immediately with the conventional top-to-bottom operation.

If a rational criterion is applied in extending the resection and a truly radical prostatectomy is the aim, then the prostate must be extirpated with the bladder neck and surrounded by all the periprostatic coverings, including Denonvilliers' aponeurosis, i.e. total extra-aponeurotic prostatectomy [13]. The operation should be conducted outside the prostatic lodge and, for the gross specimen to have a carcinological safety-margin, the lateral prostatic pedicles should be sectioned far from their posterolateral edges, with intra-operative histological monitoring of the margins of the gross specimen.

The anastomosis of the urethra and bladder is technically the most difficult and complex part of prostatectomy, with the greatest difficulties causing stenosis, fistulae and incontinence. When the urethra is cut at the level of the prostatic apex, the end of the urethra withdraws beneath the upper folium of the mid-perineal aponeurosis. Exposing it to allow careful and accurate suturing is a frustrating and very difficult task.

Different solutions have been described. A catheter may be passed to identify the urethral lumen, but this does not help to locate accurately the place for the sutures, and these may catch and damage the external sphincter. Another procedure consists of placing some sutures before sectioning the urethra completely and adding the remaining sutures afterward; however, the least unnoticed tension on these sutures causes the end of the urethra to tear.

To solve this problem, a simple manoeuvre was



developed to raise the urogenital diaphragm and draw the membranous urethra towards the surgeon, providing excellent exposure and allowing urinary continuity to be re-established with precision and with no risk of damaging the external sphincter mechanism [28]. The anatomical principles underlying the manoeuvre are that the external sphincter has no skeletal attachment, as S. Gil Vernet showed, that the striated sphincter is not integrated with the membranous urethra but covers it, and that there is a cleavage between these formations, allowing the urethra to move 1.5 cm inside the surrounding external sphincter [24].

Once the prostate has been resected, a 14 F Foley catheter is inserted into the urethra. When this emerges into the pelvic cavity, a suture is passed through the holes in its tip (Fig. 9a). The catheter is withdrawn until its tip disappears and the balloon, which is placed at the level of the bottom of the bulbar sac, is filled with 3–4 mL (Fig. 9b). The suture is then pulled toward the surgeon and when the balloon is positioned on the deep transverse muscle, it raises the urogenital diaphragm, thus causing the membranous urethra to protrude with eversion of its edges (Fig. 9c). Now the urethra can be sutured without including the fibres of the external sphincter. The needle should take up the mucosa, the layer of elastic connective tissue that encircles it and the layer of smooth muscle fibres or smooth sphincter, but not the striated sphincter.

The overall thickness of these structures is 1.5–2 mm. This manoeuvre makes it easier to place each suture carefully and accurately, as though a vascular anastomosis were being performed, at a prudent distance from

the edge, symmetrically, and with enough space between the sutures to prevent ischaemia. No more than six sutures (5/0 polyglactin, the needle proportional to the suture) should be placed, ensuring continuity without tension between the urethral and vesical mucosa. It is pointless and also dangerous to place more than six sutures or use a thicker suture, because there is a possibility of tearing and therefore a greater risk of stenosis or fistula. The anatomical and functional result depends on the quality of the anastomosis.

### Conclusions

There is still a paucity of knowledge of the history of the prostate gland in the English literature. The guidelines and strategies remain as they were half a century ago, except for some modifications or variations based on the ingenuity of a few distinguished predecessors. In 1944, Salvador Gil Vernet proposed that the nerve formations be conserved to prevent urinary incontinence and 40 years later, Walsh proposed the same to prevent erectile impotence.

The information provided by the work of Villers and Stamey re-opens the debate on the preservation of the nerve bundles. This is currently of great surgical importance, for there are proposals to preserve the cavernosal nerves, which indicates a compromise in the total extirpation of CaP. Even so, it is worth asking whether sparing these nerve formations is necessary or desirable to maintain urinary continence and/or erection in some carefully selected patients with stage B1 disease.

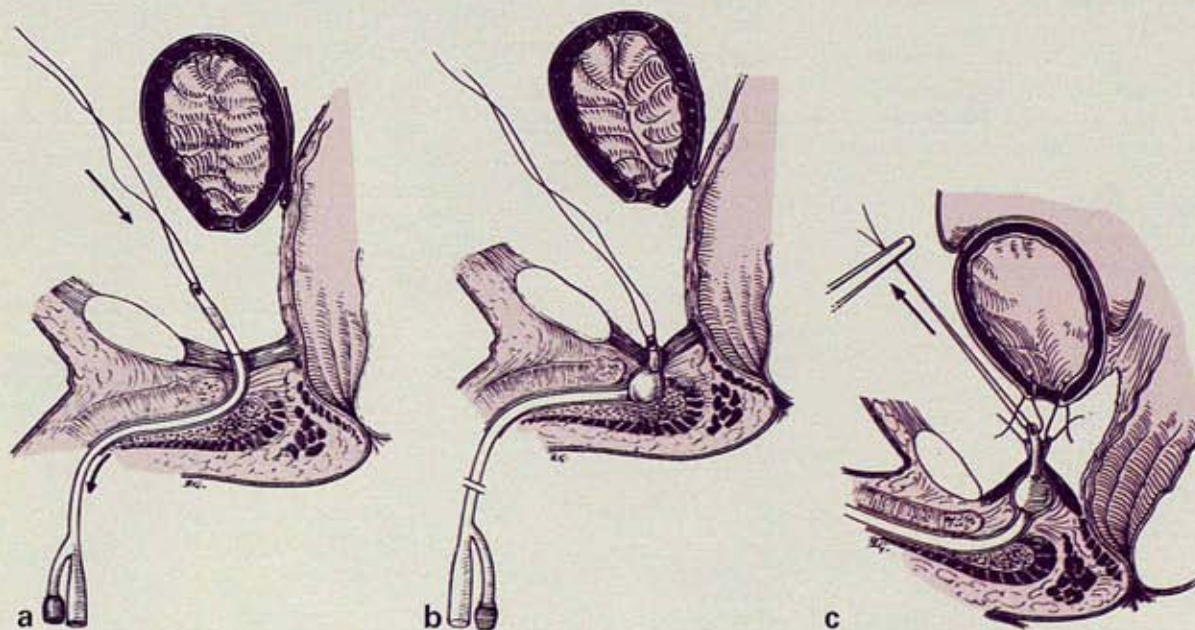


Fig. 9. a, b, c, Radical prostatectomy. Re-establishment of urinary continuity by the manoeuvre for raising the urogenital diaphragm [28].



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