UPPER LIMB SYMPATHECTOMY IN CURRENT SURGICAL PRACTICE

by

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To my

wife Ameeta,

daughter Juhi,

son Nikhail &

my teachers

ABSTRACT

Operations on the sympathetic chain have had a long and colourful history and were often considered for a disparate group of medical conditions. Currently recognised indications for sympathectomy are hyperhidrosis and Chronic Regional Pain Syndrome (CRPS). The role of sympathectomy for non-reconstructible peripheral vascular disease PVD) and Raynaud's disease not responding to medical treatment is controversial. Presently, the perceived benefits and wide availability of thorascoscopic sympathectomy has resulted in large numbers of this procedure being undertaken.

A greater understanding of the anatomy relevant to upper limb sympathectomy is appropriate given the confusing and complex arrangement of the proximal sympathetic chain. Instances of unsuccessful sympathectomy have often been attributed to the anatomical arrangement of the sympathetic chain.

The pathogenesis of conditions treated by sympathectomy is unknown; the possible aetiology of these conditions may be gleaned from the histopathological changes occurring in ganglia from patients treated successfully.

Aims

This study has 3 components :

1. **Clinical**
   - a review of the clinical experience, including a comparison of the supraclavicular and thoracoscopic approaches and evaluating the extent of sympathetic ganglionectomy.
   - anaesthetic considerations, evaluating the role of a single-lumen endotracheal tube.
   - defining the role and timing of sympathectomy for CRPS
2. **Anatomical**
   - to define the surgical anatomy appropriate to a safe and effective upper limb sympathectomy
   - to evaluate a modified anterior approach for stellate ganglion blockade (SGB)
3. **Pathological**
   - to evaluate the possibility of excised ganglia harbouring an inflammatory process using immunohistochemical techniques.

Outcome

1. Clinical

In 498 patients, a total of 939 sympathectomies were undertaken for hyperhidrosis (n=884), CRPS (n=43), Raynaud's disease (n=9) and non-reconstructable peripheral vascular disease (n= 3). When compared to the supra-clavicular approach, the thoracoscopic approach was shown to be superior in terms of safety, technical demand and cost.

A limited 2nd thoracic ganglionectomy was effective for palmar hyperhidrosis (100% and in associated axillary hyperhidrosis [81.2%] and plantar hyperhidrosis [53%]). A compensatory hyperhidrosis rate of 12.6% was noted. The single lumen endotracheal tube was found to be as effective but safer than the double lumen endotracheal tube. When undertaken early (within 3 months), the outcome to sympathectomy for CRPS was excellent

2. Anatomical

A total of 41 proximal sympathetic chains were evaluated.

Three categories of alternate neural pathways to the upper limb were defined (total incidence 90.5%). When correlated with the clinical outcome to a limited 2nd thoracic ganglionectomy, it is suggested that these alternate neural pathways are of no clinical significance.

The modified anterior SGB was always effective in blockade of the clinically significant 2nd thoracic ganglion.

3. Pathological

There is strong evidence for an autoimmune hypothesis in both primary hyperhidrosis as well as CRPS. The mechanisms responsible for the development of the symptoms in these conditions appear to be different.

DECLARATION

This study represents original work by the author and has not been submitted in any form to another University. Where use was made of the work of others, it has been duly acknowledged in the text

B. SINGH

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PREFACE

It is 110 years since the first operation on the sympathetic chain was undertaken (Alexander, 1890). The evolution of this practice has been associated with the search for the appropriate indications and a rational and safe surgical technique. The anatomy - varied and confusing at best - has long been held responsible for instances of unsuccessful sympathectomy; however, current techniques for sympathectomy are consistently successful. A re-appraisal of the relevant anatomy and the pathology of conditions successfully treated by sympathectomy is therefore timeous.

PUBLICATIONS AND SCIENTIFIC PRESENTATIONS

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1998

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CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

The history of the sympathetic nervous system – its understanding and application in surgical practice – has been a long and colourful one. Not unlike many facets of surgical development it has also suffered from misrepresentation and denial but benefited from serendipity and dogged perseverance. Indeed, the history of surgery in general is littered by acts of sheer inspiration and foresight that have transformed standard surgical procedures. Equally and sadly so, enterprising endeavours have been under-appreciated and cast aside, only to be belatedly appreciated decades later. The history of the sympathetic nervous system illustrates this with respect to its anatomical and surgical status. In formulating the current status of the sympathetic nervous system, particularly with respect to the upper limb, it is imperative to appreciate the varied contributions of our intrepid predecessors, often aided by the absence of ethical restraint.

From being originally wholly misrepresented anatomically at around the beginning of the last millennium, the sympathetic chain progressed to being accurately depicted and credited for important physiological functions (at around the mid 19th century). However, in view of the multiplicity and mutual inter-dependence of the factors which control the function of the end organ (whether blood vasculature or glandular), pin-pointing the actual cause of a specific disorder (eg. vascular disorders, causalgia or hyperhidrosis) has remained elusive. Thus the physiological, pathological and biochemical basis underlying such disorders are still in many respects far from clear; furthermore, therapeutic treatment by autonomic nerve surgery has not always been satisfactory. The turn of the 20th century saw some operations on the sympathetic nervous system being undertaken for an often disparate group of

conditions. The invariably sporadic success to sympathectomy led to the unpopularity of this approach. Genuine indications for sympathectomy were thereby relegated. However, it is equally true that symapthectomy has freed many patients from the agonizing pain of "causalgia"; it has saved in many instances, patients from ulceration or complete gangrene and amputation and it has cured many patients from the embarrassment of having a hand or foot dripping constantly with sweat. However, the greater appreciation of physiology coupled with advances in vascular surgery and pharmacotherapy, particularly from the third decade of the 20th century onwards, gradually relegated the status of sympathectomy in surgical practice.

Many patients have benefited in the past from surgery of the autonomic nervous system despite the lack of clarity in the scientific background just as patients suffering from cancer or peptic ulcers have been helped by surgery despite our ignorance about the basic causes of these diseases (Pick, 1970). With increasing numbers of sympathectomies being undertaken, afforded by the relative ease of thoracic sympathectomy, a re-evaluation of the role of sympathectomy may be timeous. The increasing experience of thoracic sympathectomy affords the opportunity to evaluate the indications for sympathectomy in current surgical practice; furthermore aspects of surgical technique (as extent of ganglionectomy, role of open sympathectomy, aspects of anaesthetic technique and timing of sympathectomy for Chronic Regional Pain Syndrome (CRPS) may also be evaluated and modified.

The anatomy of the sympathetic nervous system, though nicely diagrammed in standard texts, remains in part a veritable Pandora's Box; many questions still remain unanswered

and many traditional views are unchallenged. For decades the role of alternate sympathetic outflow to the upper limb dominated as a cause of persistent (or recurrent) activity following sympathectomy. Thus the Nerve of Kuntz (described in 1927) has been constantly stated to be an important cause of persistent sympathetic activity. In the current experience (that avoids a stellate ganglionectomy), persistent sympathetic activity does not appear to be an issue; this prompts a re-evaluation of the role of alternate sympathetic pathways. In our practice, the open approach of sympathectomy is undertaken by the supraclavicular route, effectively confining the understanding of the anatomy of the sympathetic nervous system to this approach. The increasing popularity of the thoracoscopic route prompts an evaluation of the sympathetic chain as noted on thoracoscopy. Furthermore, the pitfalls of the thoracoscopic approach also merit evaluation as does the problem of persistent and recurrent sympathetic activity following a seemingly successful sympathectomy. With a more precise anatomical background, together with a finer understanding of the function and role of the sympathetic nervous system, successful surgery on this component of the nervous system may become the rule in selected patients.

An investigation into the pathogenesis of diseases that are successfully treated by sympathectomy has not been previously undertaken. The role of the sympathetic nervous system with respect to the upper limb is largely considered to promote symptoms such as sweating (in primary hyperhidrosis and CRPS) and vasomotor changes (in CRPS and Raynaud's Disease); its role in potentiating and maintaining pain in CRPS has not been investigated. Similarly, neither has the pathogenesis nor the potentiating factor in primary

hyperhidrosis been evaluated. An investigation of the pathological mechanism for conditions successfully treated by sympathetic ganglionectomy is therefore merited.

This thesis has three components viz. clinical, anatomical and histopathological :

a) Clinical

1. The role of sympathectomy for upper limb in current surgical practice. The efficiency, complication and durability of the outcome will be considered. Given the global standpoint on sympathectomy for classic vascular diseases (vasospastic and vaso-occlusive) primary hyperhidrosis and CRPS will be considered in greater detail.
2. The most appropriate surgical approach will be defined with aspects of technique that will expedite technical ease and minimize complications, failures and enhance patient satisfaction and clinical outcome. This will include the extent of the sympathetic ganglionectomy and the most user friendly and effective surgical technique. Mechanisms responsible for an unsuccessful sympathectomy will be evaluated.

b) Anatomical

1. To define alternate sympathetic pathways applicable to the upper limb; these have long been considered as possible causes for failure of upper limb sympathectomy.
2. The arrangement of the inferior cervical, T1 and T2 ganglia in relation to the 2nd rib - considered as a key landmark for an accurate and complete upper limb sympathectomy will be evaluated.
3. Because the so-called Stellate Ganglion Block is held as pivotal in diagnosing those patients with CRPS who will benefit from sympathectomy, the anatomical basis for an accurate Stellate Ganglion Block will be defined.

c) Histopathological

1. To define the histopathologic baseline with respect to the spectrum of changes seen in hyperhidrosis and CRPS. Preliminary appraisal of ganglia from hyperhidrotic and CRPS patients has demonstrated a variable number of lymphocytes, mast cells and lymphoid aggregates with germinal centers.
2. To investigate the immunophenotype of the lymphocyte infiltrate, the intensity of this infiltration and its pathological significance.

CHAPTER 2

LITERATURE REVIEW

2.1 HISTORICAL PERSPECTIVES

> *"if the science of surgery is not to be lowered to the rank of a mere technical exercise, it must pre-occupy itself with its history"*
>
> *Emile Littre*
> *(17th C French Surgeon)*

2.1.1 ANATOMICAL PERSPECTIVE

As in many facets of medicine, an appreciation of the contributions of our predecessors is often the key to innovation and advances in surgery. The sympathetic nervous system was a totally under-appreciated structure until Galen of Pergamon (130-199 AD) drew attention to it. Unfortunately his descriptions of a common vago-sympathetic trunk arising from the brainstem remained unchallenged for centuries, a reflection of the standing and reverence of Galen's work. This anatomical misconception was perpetuated by Versalius, a renowned anatomist at Padua, at around the midway of the 2nd millennium (Figure 1). Versalius, however, established the principle of anatomical dissection that led to Eustachius demonstrating that the vagus and sympathetic trunk were separate neural entities (Versalius,1555; Russel, 1979; Royle, 1999).

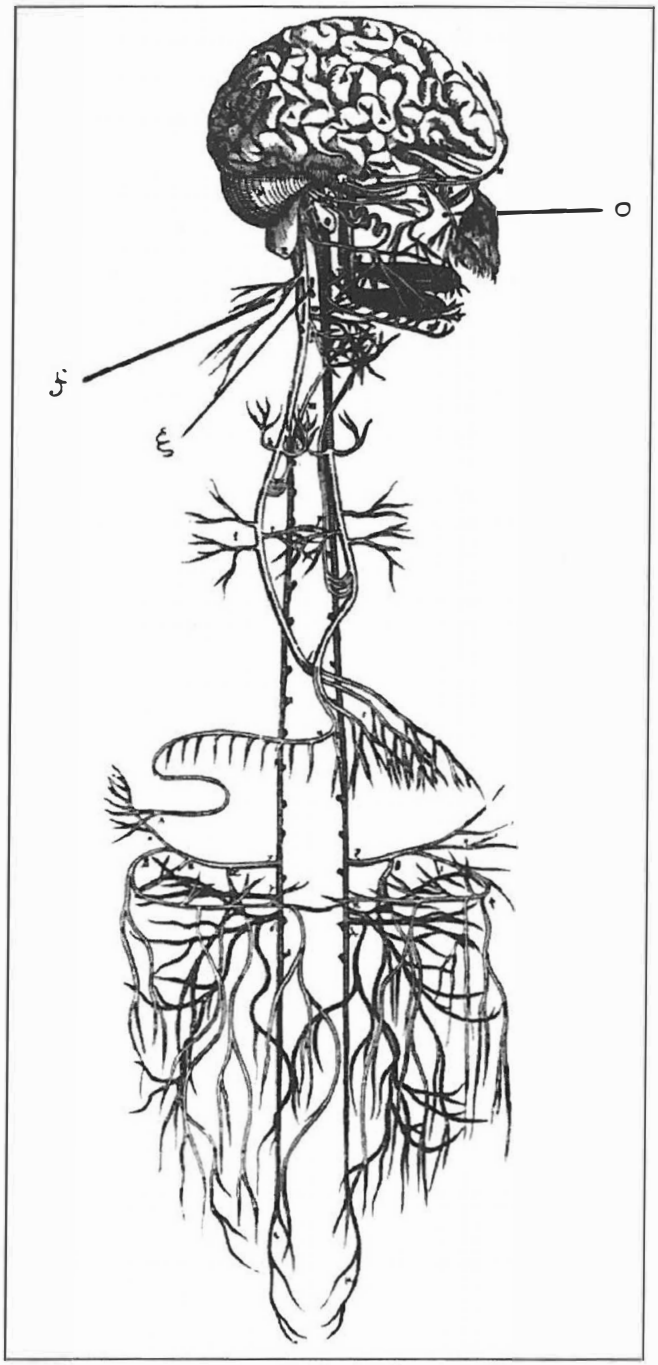


Figure 1 : *Earliest drawing of the sympathetic trunk, rami communicantes and peripheral autonomic nerves; the vagus and adjacent lower cranial nerves are also shown (Adapted from Huart and Imbault-Huar, 1980*

Winslow (1749) is credited as having named the sympathetic nerve as such (in 1732). It was suggested that nerves arising from the ganglionated trunks extending along the ventro-lateral aspects of the vertebral column supply both the intestine and the heart. By reason of the numerous connections of these trunks it was assumed that through these connections one part of the body extended influence on other parts of the body. In accordance with the then existent teaching, it was presumed that the sympathies of the body were orchestrated by these nerves. Winslow therefore called them the great sympathetics. Because he believed that the vagus and nervus intermedius subserved a similar function, he called these nerves respectively the medium and small sympathetics (Winslow, 1749; Royle, 1999).

By the end of the 18th century the anatomy of the sympathetic nervous system was fairly well defined. Greater anatomical refinements were produced by Gaskell (1886-1889) who named the chain of ganglia along each side of the spine the "vertebral or lateral ganglionic chain"; he also documented three great separate outflows of small medullated connector fibres from the central nervous system viz. a bulbar, a thoracolumbar and a sacral, forming together with the sympathetic fibres, the "involuntary nervous system." Langley and Dickinson (1889) greatly contributed to the spinal outflow and anatomical mapping of the sympathetic ganglia, elaborating upon an earlier observation of the paralysing effect of nicotine on papillay dilatation by pinpointing the action of this drug at the sympathetic ganglion cells of the superior cervical ganglion. This discovery gave Langley a tool to localise the cell station, which issued their fibres to the specific effector cells in various regions, and to map out the areas of distribution of "preganglionic to postganglionic" neurons (Pick, 1970). He classified the cervical, thoracolumbar and sacral outflows as the "autonomic nervous

system," a term he coined in 1898. In 1905, Langley observed that pilocarpine and other drugs stimulate the cranial and sacral outflows, which he then called the parasympathetic nervous system. Thus, Langley and Dickinson (1889) established the anatomical distributions of the autonomic nervous system by separating them into two great divisions (Langley and Dickinson, 1889; Pick, 1970).

The spinal origins of the sympathetic nervous system in the intermediolateral column with a localised thoracolumbar outflow was widely accepted, as was the arrangement and concept of preganglionic and postganglionic sympathetic fibres. Impetus for an even finer appreciation of sympathetic neuroanatomy came as surgical procedures were undertaken on the sympathetic nervous system. In the absence of restraining ethical committees, these pioneering and intrepid surgeons, by performing an array of procedures on the sympathetic nervous system, indirectly contributed to an even greater understanding of the sympathetic nervous system. Similarly, an understanding of the physiology of the sympathetic nervous system was often procured by serendipity.

The beginning of our understanding of the sympathetic nervous system physiology was in March 1852, when Claude Bernard and Brown Sequard serendipitously discovered the role of the sympathetic nervous system in the human circulation. Having transected the cervical sympathetic trunk at "about the middle of the neck" Bernard anticipated a fall in temperature; however, he noted "in the whole of the corresponding side of the rabbit's head a striking hyperactivity in the circulation, accompanied by increase in warmth" This observation, a reversal of Bernard's hypothesis, inadvertently prompted operations on the sympathetic nervous system for the management of vasculopathies some four decades later (Bernard, 1852; Pick, 1970).

TABLE 1 : THE SYMPATHETIC NERVOUS SYSTEM – HISTORICAL LANDMARKS

YEAR	AUTHOR	DESCRIPTION
130-200 AD	Galen	original anatomic dissection and documentation of a vago-sympathetic trunk (part of 6th cranial nerve) described superior,inferior cervical,semi-lunar ganglion and rami communicantes
1555	Vesalius	did not challenge Galen's "6th nerve "
1564	Eustachius	considered vagus and sympathetic as different
1664	Willis	described sympathetic trunk as "intercostal" with an intracranial origin demonstrated cervical ganglia and rami communicantes
1727	Pourfour du Petit	suggested "intercostal" nerves originate below cranium ie the spinal origin of the sympathetics
1732	Winslow	described 3 "sympathetic nerves" viz "small" (facial nerve) "middle" (vagus), "large" (sympathetic)
1751	Meckel	regarded ganglia as stations wherein nerve bundles are sorted prior to dispersal to terminations.
1764	Johnstone	regarded ganglia as "little brains"
1800	Bichat	described sympathetic trunk as "chain of little brains", noting some rami to be white, others grey
1846	Beck	ganglia connected with cervical and sacral nerves by grey rami only
1852	Claude Bernard	described vasoconstrictor function of the sympathetics
1852	Brown-Sequard	cooling of skin and diminution of blood flow on stimulation of the sympathetics
1854	Remak	comprehensive account of the histology of sympathetic ganglia. Observed that preganglionic, white rami contained only myelinated fibers and postganglionic, grey rami contained myelinated and unmyelinated fibers
1874	Frey	described the sympatheic innervation of upper limb vessels
1877	Bernard	ventral spinal roots contain efferent sympathetic fibers to the gastro-intestinal tract, iris, bladder, salivary glands and blood vessels. Visceral efferents mediate reflexes over the spinal cord
1885	Gaskell	sympathetic communicates to spinal cord exclusively via white rami. Spinal origin of sympathetic from cells in lateral horn. Efferent fibres to trunk (by white rami) only in thoraco- lumbar region
1898	Langley	cranial, thoracolumbar and sacral outflow comprises the autonomic nervous system. Saw a functional antagonism between sympathetics and parasympathetics. Described pre- and post-ganglionic neurons, using the paralyzing effect of nicotine on sympathetic ganglia

1914	Kramer and Todd	sympathetic fibres do not reach periphery along main vessels but run with sensory nerves to join arteries at successive levels
1927	Kuntz	demonstration of an intrathoracic ramus that was considered to be an alternate neural pathway to the upper limb
1936	Smithwick	preganglionic fibres to upper limb emerge below the 1st thoracic segment of the spinal cord
1939	Foerster	division of trunk between 2nd and 3rd thoracic ganglion produced denervation of vascular structures of the upper limb
1942	Hyndman & Wolkin	2nd thoracic ganglion pivotal to upper limb sympathetic supply
1946	Pick & Sheehan	ganglia designated according to the number of the vertebrae
1953	Mitchell	lateral gray column of spinal cord provides origin of preganglionic fibers
1959	Wrete	numbered ganglia according to intercostal space
1960	Jit & Mukerjee	reported 11 ganglia in 71% of cases; 12 ganglia in 23% of cases; 10 ganglia in 4% of cases and 13 ganglia in 20% of cases
1970	Pick	reported that ganglia ranged in numbers between 9 and 13
1971	Hollingshead	described only 11 thoracic ganglia
1976	Gabella	ganglia either para-vertebral (along ventrolateral aspect of spinal column) or pre-vertebral (close to median plane of body)
1987	Groen et al.	ganglia ranged between 8 – 10 in number

Because the nuances of the physiology of the sympathetic nervous system as we currently appreciate were lacking, indications for surgery on the sympathetic nervous system, not surprisingly, were discordant. This, coupled with a less than clear appreciation of the anatomy, the absence of a censorial surgical milieu and willing patients, led to operations on the sympathetic nervous system being undertaken for a disparate group of conditions. Thus, desperately, sympathectomy was undertaken to alleviate a variety of conditions for which there was no efficient treatment at the time. The first surgeon to operate on the sympathetic nervous system was Alexander of Liverpool; he performed a cervical sympathectomy for epilepsy in 1889. Jonnesco of Bucharest (1896) undertook sympathectomy for exophthalmic goitre; as reported by

Drott (1994), sympathectomy was also undertaken by Abadie (1899) for glaucoma, Pappalado (1902) for trigeminal neuralgia and Ball (1905) for optic nerve atrophy. Not surprisingly, the outcome to sympathectomy for these conditions was invariably unsatisfactory.

Perhaps of prescient significance was the endeavour by Jaboulay in 1899. He, mindful of Bernard's observations some four decades earlier, undertook peri-arterial sympathectomy for the so-called spastic vascular disorders. This procedure did not gain prominence until his protégé , Rene Leriche (1913), gave it greater publicity. Peri-arterial sympathectomy did not prove to be an enduring surgical option. An anatomical basis for failure after peri-arterial sympathectomy was presented by Kramer and Todd (1914) who demonstrated that the sympathetic fibres do not reach the periphery along the main vessels, but run with the sensory nerves to join arteries at successive levels. The endeavours of Jaboulay and Leriche, notwithstanding the enormous contributions to the understanding and clinical applications of surgery on the sympathetic nervous system, represented a timely departure from the developing trend of cervical ganglionectomy (including superior and middle ganglionectomy).

Bruning (1923) was one of the few to have used peri-arterial sympathectomy extensively for the treatment of Raynaud's phenomenon and scleroderma. He therefore suggested extirpation of the stellate ganglion in order to interrupt all the sympathetic fibers before they join the spinal nerves. He subsequently reported excellent immediate results in several cases of Raynaud's phenomenon and scleroderma. Within the next few years various authors (Royle, 1924; Adson and Brown, 1929; Davis et al., 1926) started to employ ganglionectomy for the treatment of Raynaud's phenomenon.

The years of invariably inappropriate surgical endeavours finally ended when Kotzareff (1920) performed a cervical ganglionectomy (he excised two cervical ganglia under local anaesthesia) in a patient with primary hyperhidrosis of the face and upper limbs. The operation was a success despite the Horner's syndrome. The ensuing years saw the further refining of the indications for sympathectomy and, with this, an appreciation of the anatomy in order to obtain a complete sympathectomy. In addition to primary hyperhidrosis, vasospastic disorders were also considered then to be a valid indication for sympathectomy. The treatment of causalgia was added to these, when, in 1930, Spurling reported the successful treatment of this condition by cervico-dorsal sympathectomy.

The rapid emergence of peripheral and cardiovascular surgery and its wide availability together with the development of new pharmacological agents during the 1940s and onwards saw the gradual decline of sympathectomy as a relevant surgical technique. However, the pharmacological treatment of palmar hyperhidrosis and, on occasions, CRPS (previously called causalgia) have been shown to be unimpressive. Furthermore, the effect of relegating sympathectomy saw the avoidance of the critical evaluation of this operation. Lack of clinical interest also impacted negatively on the further anatomical evaluation of the sympathetic nervous system; thus the contributions to its understanding over the past fifty years have largely not matched those up to the 1940s.

2.1.1.1 Spinal Sympathetic Outflow To The Upper Limb

The exact preganglionic sympathetic outflow from the spinal cord in humans was determined physiologically by recording the electrical activity of peripheral nerves during stimulation of the ventral roots of the spinal cord and recording changes in skin resistance (Geohegan and Aidar, 1942). The lateral grey column of the thoracic segment of the spinal cord provides the origin of the sympathetic nerves cells responsible for the sympathetic preganglionic fibers (Mitchell, 1953). The precise extent of the spinal preganglionic outflow is a vexed issue; Telford (1935) and Smithwick (1936) demonstrated that the preganglionic fibers for the upper limb emerged in white rami communicantes below the level of the 1st thoracic segment of the spinal cord. White and Smithwick (1952) suggested that "it is not necessary to divide the 1st thoracic white ramus; it does not carry vaso-or sudomotor fibres of importance to man." Simmons and Sheehan (1939), Goetz and Marr (1944), Palumbo (1956) and Barcroft and Swan (1953) re-affirmed this view, finding no sympathetic activity in man when the outflow from the 1st thoracic segment is not divided.

The distal limit of the outflow of preganglionic sympathetic fibres to the upper limb is largely inconclusive (Hoffman, 1957). The view that all preganglionic fibers to the upper limb traversed the nerve roots distal to the thoracic ganglion was supported by Gask (1934), Foerster (1939), Sheehan and Marrazzi (1941) and Geohegan and Aidar (1942). Smithwick (1940), White et al. (1952) suggested that the upper spinal origin of the upper limb sympathetic outflow was at the level of the 2nd thoracic spinal root. The spectrum of the spinal origin of the upper limb sympathetic supply as suggested by various authors is demonstrated (Figure 2); Ray (1943, 1953) demonstrated that the

spinal outflow may be higher, including the 1st thoracic or even the 8th cervical spinal root. Bridges and Yahr (1955) and Hoffman (1957) suggested that the upper limit for preganglionic outflow may b as high as the 8th cervical segment. Similarly the lower limit of spinal outflow is also controversial; it is placed between the 7th to 10th thoracic spinal segments.

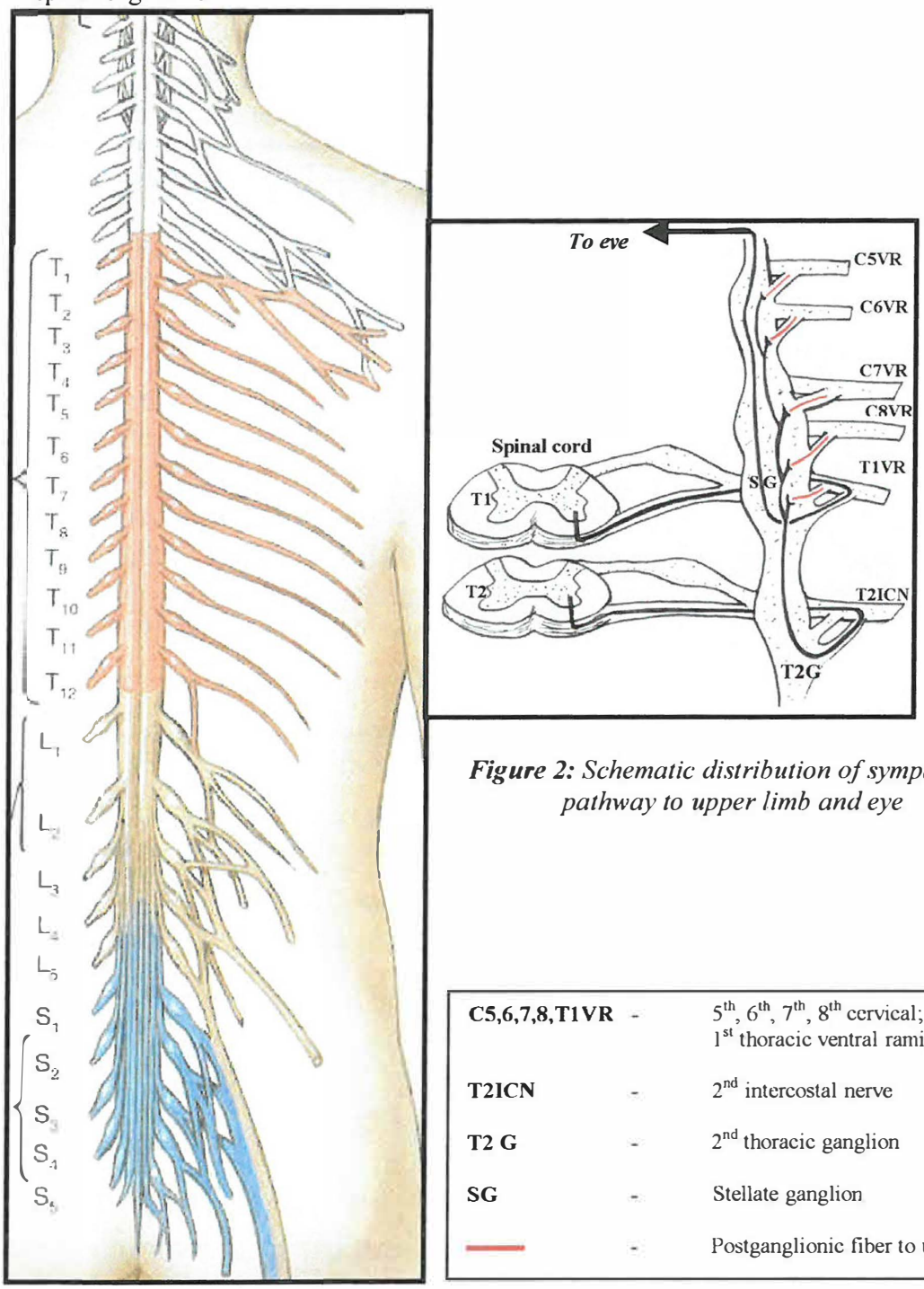


Figure 2: *Schematic distribution of sympathetic pathway to upper limb and eye*

C5,6,7,8,T1VR	-	5th, 6th, 7th, 8th cervical; 1st thoracic ventral rami
T2ICN	-	2nd intercostal nerve
T2 G	-	2nd thoracic ganglion
SG	-	Stellate ganglion
———	-	Postganglionic fiber to upper limb

The failure to precisely define the extent of the spinal origin of upper limb sympathectomy outflow impacted on the extent of sympathectomy to effect upper limb sympathetic denervation. Emphasis on the spinal segments or the spinal root rather than the level of the ganglionectomy in effecting sympathetic outflow, may have contributed to this dilemma. Thus, Foerster (1939) on the basis of stimulation of ventral nerve roots and plethysmographic studies concluded that the 3rd to 7th thoracic preganglionic fibres were concerned with the sympathetic innervation of the upper limb; he suggested that the division of the sympathetic chain between the 2nd and 3rd thoracic ganglia produced denervation of the vascular structures of the upper limb. In contrast, Hyndman and Wolkin (1942) advocated removal of the 2nd thoracic ganglion alone. Atlas (1941), Richards (1946) and White et al. (1952) reported that some sympathetic activity persisted in the hand following removal of the sympathetic chain below the 2nd thoracic ganglion. The reports of Ray (1943), Lazorthes (1949), Thompson (1950) and Haxton (1947) and Pick (1970), who all found evidence that vasomotor fibres to the upper limb emerged in the 1st thoracic nerve root, ensured that the issue remained a controversial one. Indeed, Foerster (1936), Smithwick (1936), Telford (1935) and Hyndman and Wolkin (1942) argued that the 1st thoracic spinal nerve did not contain sympathetic fibres to the upper limb.

The increasing success with limited sympathectomies (2nd thoracic ganglionectomies) for upper limb sympathectomy has essentially resolved this issue (O'Riodian, 1993); it is clear, regardless of the spinal origin of the sympathetic outflow, that the 2nd thoracic ganglion is pivotal for upper limb sympathetic innervation. Large clinical series of 2nd thoracic ganglionectomy have shown that this approach is adequate for upper limb sympathetic denervation, reinforcing the view of Hyndman and Wolkin (1942). The role

of alternate neural pathways, originally described by Kuntz and long considered an important cause of an unsuccessful operation, merits a re-evaluation in the light of the large numbers of sympathectomies presently undertaken.

2.1.2 SURGICAL PERSPECTIVE

The pioneering surgical endeavours of the sympathetic nervous system were associated with an unpredictable outcome. Although often associated with an inappropriate indication; the increasing surgical endeavours on the proximal sympathetic chain prompted further re-appraisal of the anatomy of this component of the sympathetic chain. Table 2 chronicles the evolution of indications and techniques for upper limb sympathectomy until the 1990s.

TABLE 2 : EVOLUTION OF INDICATIONS AND TECHNIQUES FOR SYMPATHECTOMY (UP TO 1993)

YEAR	AUTHOR	PROCEDURE	CONDITION
1889	Alexander	Superior cervical ganglionectomy	Epilepsy
1892	Jacksch	Reserted vertebral plexus : divided trunk between mid and inferior ganglion	Epilepsy
1896	Jonnesco	Divided trunk above and below mid ganglion	
1899	Jaboulay	Peri-arterial sympathectomy	Trophic vascular disorders
1899	Abadie	Superior cervical ganglionectomy	Glaucoma
1902	Pappalado	Superior cervical ganglionectomy	Trigeminal neuralgia
1905	Ball	Superior cervical ganglionectomy	Optic nerve atrophy
1913	Leriche	Peri-arterial sympathectomy	Raynaud's Disease
1917	Leriche	Peri-arterial sympathectomy	'Causalgia'
1920	Kotzareff	Superior and mid ganglionectomy	Hyperhidrosis
1921	Jonnesco	Mid and inferior ganglionectomy	Angina
1924	Royle	Stellatectomy	Raynaud's Disease
1930	Spurling	Cervico-dorsal sympathectomy	'Causalgia'
1924	Henry	Stellatectomy (post approach)	Angina
1929	Adson	Stellatectomy and upper dorsal sympathectomy	Raynaud's Disease
1935	Telford	2^{nd} and 3^{rd} ramusectomy; trunk transected below 3^{rd} ganglion	Raynaud's Disease
1936	Smithwick	Preganglionectomy and transection of trunk	Raynaud's Disease
1942	Hughes	Endoscopic stellatectomy	Raynaud's Disease and Causalgia
1942	Hyndman and Wolkin	2^{nd} thoracic ganglionectomy	Raynaud's migraine
1944	Goetz and Marr	Transthoracic and endoscopic 2^{nd} thoracic ganglionectomy	Raynaud's Disease
1954	Kux	Various endoscopic operations on the 'vegetative' nervous system i.e. sympathetic and parasympathetic (vasotomy) [German]	
1969	Cloward	Dorsal midline approach for bilateral sympathectomy	Hyperhidrosis
1971	Roos	Transaxillary, extrapleural with 1^{st} rib resected	
1978	Kux	Endoscopic 2^{nd} to 6^{th} thoracic ganglionectomy	Hyperhidrosis
1990	Byrne et al.	Endoscopic 2^{nd} to 4^{th} ganglionectomy	Hyperhidrosis
1991	Claes and Gothberg	Endoscopic sympathectomy	Hyperhidrosis
1993	O'Riordan	2^{nd} thoracic ganglionectomy (Telford approach)	Hyperhidrosis
1993	Chandler	VATS; 2^{nd} and 3^{rd} thoracic ganglionectomy	'Causalgia'
1993	Krasna	Video assisted thorascopic sympathectomy (VATS); 1^{st} to 3^{rd} thoracic ganglionectomy	Hyperhidrosis
1998	Lin et al.	Thoracoscopic clipping of sympathetic chain	Hyperhidrosis

Of significance was Kuntz's demonstration (1927) of a nerve by-passing the 2nd or 3rd thoracic ganglion to the brachial plexus. In the context of obviating a failed sympathectomy, this nerve - then reported to be present in up to 10% of humans - was considered to be of crucial importance. Additional sympathetic nerves that reached the brachial plexus via the sinu-vertebral nerve (van Buskirk, 1941) or the vertebral plexus were also described. The latter originates from a large branch of the stellate ganglion ; rami communicantes from this plexus may join the ventral rami of the upper five or six cervical spinal nerves (Williams et al., 1995). With continual clinical experience it also became apparent that effective upper limb sympathectomy could be undertaken without cervical (including the stellate ganglion) ganglionectomy and that ganglionectomy at the level of the 2nd thoracic ganglion (and cephalad) was effective. (Hyndman and Wolkin, 1942; Atlas, 1941; Goetz and Marr, 1944).

Despite these refinements in the understanding of the upper limb sympathetic supply, the surgical approach remained a vexed issue. Several surgical techniques were described during the late 1920's and early 1930's. These techniques not only employed different approaches (anterior cervical, anterior thoracic or posterior extra-pleural), but also different forms of handling of the sympathetic chain ranging from resection of the stellate ganglion with or without segments of the upper thoracic sympathetic chain. Leriche (1926) was the first to use an anterior approach for the resection of the stellate ganglion. Royle (1932) performed stellectomy through a 5cm skin incision across the insertion of the sternocleidomastoid muscle. Gask (1934) modified these approaches, using a collar incision to undertake the bilateral resection of the stellate ganglion and the 2nd thoracic ganglion. Telford (1935) used essentially the same technique as Gask;

however, the stellate ganglion was left intact, the white rami of the 2nd and 3rd thoracic nerves were divided and the sympathetic chain crushed below the 3rd thoracic ganglion.

The posterior extra-pleural approach by rib resection was first introduced by Henry (1924) for the unilateral removal of the stellate ganglion. Adson and Brown (1929) and Adson (1931) described an operation for the bilateral resection of the stellate ganglion and upper thoracic sympathetic ganglia. Smithwick (1936) advocated a pre-ganglionic sympathectomy- rather than ganglionectomy- for optimal sympathetic denervation. The premise for this was based on the observation that recurrent sympathetic activity was approximately three times greater than following a pre-ganglionic section (Ascroft, 1937). It became apparent that the sympathetic nerves had great ability to regenerate following transection or resection, leading to recurrent sympathetic activity. To this end Smithwick (1936, 1949) devised a preganglionic section of the sympathetic chain. The white and grey rami of the 2nd and 3rd thoracic ganglia together with their respective intercostal nerves were transected; the sympathetic chain was transected below the 3rd ganglion and sutured to muscles. The effectiveness of this approach was not reported. If anything, this elaborate approach depicts the challenges posed to our innovative, pioneering surgical forefathers. Indeed, procuring an effective and reproducible operation to effect upper limb sympathectomy long remained a holy grail to the surgeon; to this end a variety of approaches evolved since sympathectomy had become a viable and essential operation (Table 3, Figure 3).

TABLE 3 : THE SPECTRUM OF APPROACHES FOR UPPER LIMB SYMPATHECTOMY

TYPE OF APPROACH	AUTHOR
Anterior Supraclavicular	Telford (1935) Bogokowsky et al. (1983) Keaveny et al. (1977)
Posterior Paravertebral	Golueke et al. (1988)
Posterior Midline	Cloward (1969)
Anterior transthoracic	Goetz and Marr (1944) Palumbo (1956)
Axillary transthoracic :	Atkins (1954)
Axillary transthoracic with 1st rib resection	Roos (1971)
Minimally invasive sympathectomy Endoscopic Video-Assisted	 Hughes (1942) Goetz and Marr (1944) Kux (1954) Chandler (1993) Chao et al (1993)

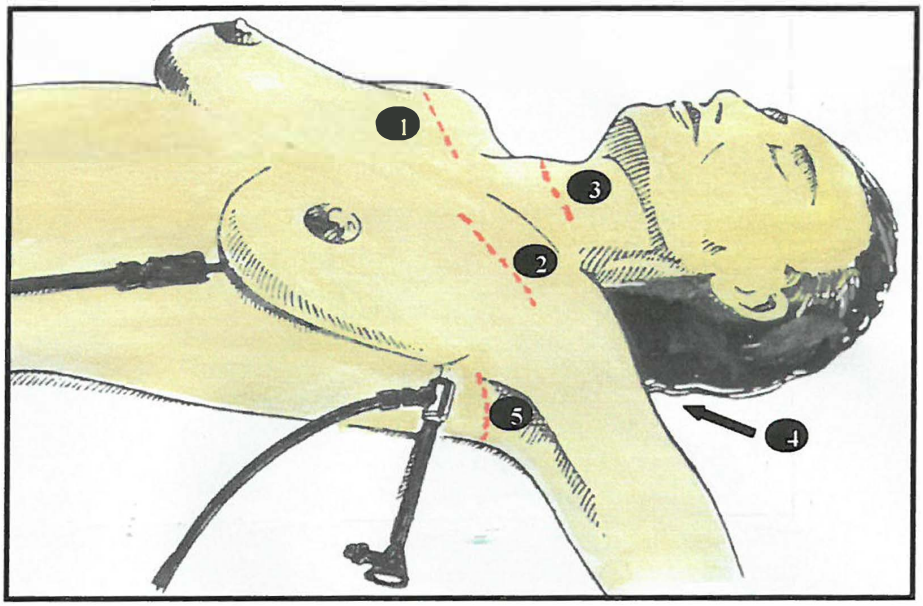


Figure 3 : *Surgical options for sympathectomy*

1- Garry (1949), **2** – Palumbo (1956), **3** – Lougheed (1965), **4** – Cloward (1969), **5** – Roos (1971)

From South Africa, Goetz and Marr (1944) described the trans-thoracic approach via an incision over the 1st or 2nd intercostal space about 4 inches in length, commencing at the margin of the sternum; in the same communication the authors drew attention to the possibility of the thoracoscopic approach. Atkins (1954) modified this to an axillary trans-thoracic approach. Palumbo (1956) re-appraised the anterior trans-thoracic route in 1966, advocating access to the sympathetic chain via the 3rd or 4th intercostal space. Although providing the best exposure, the trans-thoracic approach evokes the morbidity and sometimes the mortality of a thoracotomy.

Cloward (1969) described the dorsal midline approach which gives access to both sides. This approach has been particularly popular among neurosurgeons. Roos (1971), in modifying the Atkin's axillary trans-thoracic approach, described an extra-pleural approach after trans-axillary resection of the 1st rib. This approach gained popularity among vascular surgeons.

Regardless of the open technique favoured, these are invariably technically demanding procedures which, apart from leaving sizeable scars, often require several days of recovery in hospital and weeks or months delay in resuming normal activity. The variety of surgical approaches to affect upper limb sympathectomy attest to the failure by surgeons to find a safe, user friendly and universally reproducible surgical approach. The supraclavicular approach popularised by Telford (1935) is arguably the most widely used of the available "open" surgical approach. This is probably reflective of the tradition that defines "cervical sympathectomy" as primarily a vascular procedure; vascular surgeons are facile with this approach which also affords ready access to the thoracic outlet.

Notwithstanding this, the choice of the surgical approach has largely been a subjective one : no comparative trial has been undertaken to justify the suitability of a particular approach. This is of particular importance given the popularity of the thoracoscopic approach. Since Jacobeus (1922) first passed a cystoscope into the pleural space for diagnostic purposes and Hughes (1942) initial report of a sympathectomy undertaken at thoracoscopy, this approach had often fallen into obscurity. This, despite the enormous experience of Kux - widely regarded as the father of thoracoscopic surgery - who reported his experience of over 1400 sympathectomies (and vagotomies) in 1954. His thoracoscopic technique was largely confined to the German speaking countries during the following decades (Kux, 1954).

The endoscopic approach was however reported sporadically, the most impressive of these being by Byrne (1990). Employing standard equipment, Byrne emphasized the ease of this approach; this was at the dawn of the minimal access surgery era. The subsequent advances in optics, video-technology and illumination proved to be a major boost for the thoracoscopic technique. The wide availability of necessary instrumentation coupled with the refinements of basic minimal access surgical skills has rapidly installed the thoracoscopic approach as an invaluable technique to effect upper limb sympathectomy.

Refinements in the thoracoscopic technique have continued with the description of two millimeter ports that have provided even better cosmesis without the loss of technical benefit (Yim, 2000; Kao, 2001).

In order to diminish the troublesome problem of compensatory hyperhidrosis following the excision or cautery of the sympathetic ganglion, clipping of the sympathetic chain

without the transection of the ganglion or its branches has been advocated. This technique, it is suggested, interrupts the sympathetic outflow and has the appeal of restoring the original sweating distribution on removal of the clips if unpleasant effects follow the original clipping procedure (Lin, 1998).

2.2 CLINCAL PERSPECTIVES

2.2.1 INDICATIONS

A greater appreciation of the anatomy and physiology of the sympathetic nervous system coupled with the clinical experience with sympathectomy harnessed during the course of the previous century has helped crystallize the indications for upper limb sympathectomy. The primary indications are primary hyperhidrosis and, increasingly, CRPS. The advances in reconstructive vascular surgery and pharmacotherapy had made sympathectomy an adjunctive in therapeutic option for occlusive vascular disease and vasospastic disorders.

2.2.1.1 PRIMARY HYPERHIDROSIS

Sweating is a natural phenomenon necessary for the regulation of an individual's body temperature. The secretion of sweat is mediated by a portion of the vegetative nervous system (the sympathetic nervous system). In some people (approximately 1% of the population), this system is working at a very high activity level, far higher than needed to keep a constant temperature. The incidence is generally higher amongst infants, teenagers and young adults; this is probably reflective of the social implications of hyperhidrosis. Although both sexes are equally affected, females may find this condition less acceptable.

CLASSIFICATION AND CAUSES

Causes

- *Primary or essential (idiopathic)*

This is a far more frequent condition than secondary hyperhidrosis and appears, generally, to be localized in one or several locations of the body (most often hands, feet, axillae or a combination of them). It usually starts during childhood or adolescence and persists throughout life. It has been suggested that nervousness and anxiety can elicit or aggravate sweating, but psychological or psychiatric disturbances are only rarely causes of the disorder.

- *Secondary (as part of an underlying condition)*

Some conditions can promote excessive sweating, as a rule, involving the whole body. Listed are some of the predisposing conditions :

- ***physiological*** : emotional factors, hot environment, over-clothing, exercise
- ***febrile illness***
- ***endocrine and metabolic disorders :*** thyrotoxicosis, diabetes mellitus, hypoglycaemia, acromegaly, phaeochromocytoma
- ***drugs and substance abuse :*** acetaminephen, aspirin, insulin, anti-emetics, morphine, bethanecol, pilocarpine, mercury poisoning and narcotic withdrawal
- ***cardiovascular disorders :*** myocardial infarction, congestive cardiac failure
- ***respiratory failure***

Although neither a life nor limb threatening condition, primary palmar hyperhidrosis may have acute social implications. This is underscored by Charles Dickens (ever the

diagnostician with an unerring eye for detail) description of palmar hyperhidrosis in the fictional character, Uriah Heep, the conniving clerk with cold clammy hands in his classic, "David Copperfield". Uriah Heep arguably developed as one of the most celebrated scoundrels in English literature. His most distinctive physical features were cold, sweaty palms and lank hands, "like a fish". Uriah was portrayed as an obsequious, hypocritical and manipulative character.

> *"...As I came back, I saw Uriah Heep shutting up the office, and feeling friendly towards everybody, went in and spoke to him, and at parting, gave him my hand. But oh! What a clammy hand his was! As ghostly to touch as to the sight! I rubbed mine afterwards, to warm it, and to rub his off. It was such an uncomfortable hand that, when I went to my room, it was still cold and wet upon my memory..."*
>
> *"...I found Uriah reading a great fat book, with such demonstrative attention, that his lank forefinger followed up every line as he read and many clammy tracks along the page (or so I fully believed) like a snail..."*
>
> *"... He frequently ground his palms against each other as if to squeeze them dry and warm, besides often wiping them, in a stealthy way, on his pocket handkerchief..."*
>
> *-David Copperfield, chapter 11, by Charles Dickens*

The repulsive nature of the Uriah character probably impacts on the sufferers of primary hyperhidrosis leading to embarrassment, psycho-social trauma and physical discomfort (Carter, 1994).

The aetiology of primary hyperhidrosis is unclear. Issues such as ethnicity, geographic factors (eg altitude, humidity, coastal location) have not been seriously considered. It has been suggested that up to 40% of sibling or other first or second degree family members have a similar condition. Though presently unproven, genetic factors may play a role in primary hyperhidrosis (Mares, 1996). The condition is universally distributed. Large series have been reported from South East Asia, Israel and Europe (Table 4). In South Africa primary hyperhidrosis has been known to be fairly common in the Durban region. To date, there has been no audit on the presentation and management of

hyperhidrosis from a South African centre. Significantly, there has been no reports on the incidence and management of hyperhidrosis from elsewhere in Africa.

TABLE 4 : *PALMAR HYPERHIDROSIS : WORLD WIDE SERIES*

LOCATION	PATIENT NUMEBRS	OPERATION	PERIOD OF STUDY	AUTHOR
Tel Aviv	475	Open	1968-1992	Adar (1994)
Boras (Sweden)	602	Thoracoscopic	1987-1992	Gothberg (1994)
London (UK)	50	Thoracoscopic	1986-1991	Edmondson et al. (1992)
Taiwan	150	Thoracoscopic	1991-1992	Chih (1993)
Cork, Ireland	94	Open	1978-1990	O'Riordain (1993)
Vienna	323	Thoracoscopic	1965-1992	Herbst (1994)
Taipei, Taiwan	450	Thoracoscopic	1991-1994	Kao (1994)
Tainan, Taiwan	719	Thoracoscopic	1989-1992	Lee (1994)
Vienna	63	Thoracoscopic	1974-1976	Kux (1978)
Durban, RSA	103	Thoracoscopic	1992-1994	Singh et al. (1996)
Dublin, Ireland	112	Thoracoscopic	1980-1990	Byrne (1990)
Haifa, Israel	85	Open	1975-1990	Hashmonai (1992)

MANIFESTATIONS OF PRIMARY HYPERHIDROSIS

Palmar hyperhidrosis : This is by far the most distressing location since hands are more exposed in social and professional activities than any other part of the body.

Axillary hyperhidrosis : This may cause embarrassing wet marks to the clothing as well as some discomfort; however it is less distressing than palmar hyperhidrosis

Plantar hyperhidrosis : Though less distressing than palmar hyperhidrosis, plantar hyperhidrosis leads to bromhidrosis, blisters, infections and rotting of socks and shoes

Facial hyperhidrosis : Sweat pouring down from the forehead in conditions of stress can be very distressful, inducing the patient to think that others may consider him or her to be insecure.

Individuals invariably present with a combination of the above categories; not surprisingly it is the palmar component of this condition that drives the patient to seek help. Sweating presents spontaneously without provocation. It is seldom continuous.

TREATMENT

Primary hyperhidrosis may be managed by a variety of techniques directed specifically at reducing the sweating to an acceptable level or abolishing it altogether. Non-operative approaches include local measures such as the application of topical agents (aluminium chloride, glutaraldehyde and tannic acid), iontophoresis, systemic anti-cholinergic medication and psychotherapy. Operative treatment includes excision of axillary sweat glands, suction assisted lipolysis and sympathectomy (Moran and Brady, 1991).

Local Measures : Patients with plantar hyperhidrosis should apply an absorbent foot powder; leather shoes and cotton or woollen socks should be worn, avoiding rubber and synthetic materials (Moran and Brady, 1991)

Topical agents : Aluminium chloride (20-25%) in 70-90% alcohol is the most widely used. Varying success rates for the treatment of hyperhidrosis has been reported (Scholes, 1978; Perdikis, 1988). It may work by obstructing the sweat gland pore or causing atrophy of the secretory cells. Treatment is limited by some degree of axillary irritation. Tanning agents, gluaraldehyde and tannic acid may also be effective but are associated with brown staining that preclude their use (White, 1986).

Iontophoresis : This procedure, which coagulates eccrine sweat glands electrically, can be used to treat palmar and plantar hyperhidrosis. A direct current of 15-30 mA supplied by a galvanic generator is applied to the palms and soles immersed in an electrolyte solution. The initial treatment lasts for twenty minutes and treatment may be repeated

for three to six times weekly until the desired results are obtained. Maintenance treatment can be performed as frequently as necessary (Shrivastava and Singh, 1977; Reinauer et al., 1993).

Drugs : Systemic anti-cholinergics may be effective but unpleasant side-effects such as blurred vision, dry mouth and urinary retention preclude their use (Moran and Brady, 1991).

Psychotherapy : This has a very limited effect in the majority of patients. Psychological problems are in most cases a consequence of hyperhidrosis and not the cause (Greenhalgh, 1971).

Botulinum toxin : Treatment of hyperhidrosis by intracutaneous Botulinum toxin is a recent non-surgical option. Botulinum is a potent neurotoxin that blocks cholinergic nerve terminals (Ambache, 1951). Several studies have shown its effectiveness in reducing palmar hyperhidrosis in the short term. A multicentre trial of Botulinum toxin showed this therapy to be effective and safe. Several (strictly) intracutaneous injections are necessary at one sitting after the identification of the hyperhidrotic areas by the minor iodine starch test . The treatment has to be repeated within 4-6 weeks of the initial therapy. Furthermore, mild transient muscle weakness of the hand may occur. Relapses and non-response to further botulinum therapy may occur, due to the development of neutralising antibiotics (that may develop with deeper injection of the botulinum injection) (Kessier, 1999). Whilst seemingly effective in the short term, further studies are needed to define the optimal dose and frequency of injections and thereby establish the role of this treatment in the management of hyperhidrosis (Karamfilov et al., 2000).

The spectrum of non-operative options attests to the failure of anyone of these being consistently successful. Surgical options include excision of the axillary sweat glands

and sympathectomy. Patients with axillary hyperhidrosis who are unresponsive to medical therapy can be effectively treated by excision of the axillary sweat glands. The area of greatest concentration of eccrine sweat glands corresponds to the hairy portion of the axilla and can be accurately identified by starch iodine test. The simplest method involves excision of this outlined area (Hurley and Shelley, 1963). Excision of the axillary sweat glands may prove to be unattractive option because repeated and more extensive excisions may be necessary resulting in the formation of hypertrophic and/or constrictive scars (Stenquist, 1985). Presently, sympathectomy is the treatment for palmar hyperhidrosis; a definitive cure rate of nearly 100% is widely reported. This outcome is also noted to be enduring. Furthermore, associated axillary hyperhidrosis may also be successfully treated by sympathectomy. Whilst sympathectomy may be undertaken by a variety of techniques the thoracoscopic approach is widely considered to be a safe, easy and successful option (Kao, 1994; Lin, 1990; Singh, 1996). Employing basic minimal access surgical techniques, complications are minimal. The chief concern with sympathectomy for the treatment of hyperhidrosis is the issue of compensatory hyperhidrosis which may occur in up to 64 % of patients (Byrne,1990). The cause of compensatory hyperhidrosis is obscure. Guttman (1940) suggested it to be a compensatory response associated with heat response ; Monro (1960) attributed it to a special supraspinal reflex whilst Shelley and Florence (1960) suggested that compensatory hyperhidrosis served a thermoregulatory function. Regardless of its aetiology, compensatory hyperhidrosis may be a devastating effect of sympathectomy with some patients regretting the procedure. The impact of a limited (2^{nd}) ganglionectomy as opposed to an extended (2^{nd} to 4^{th} ganglionectomy) is unclear. The effect of a limited 2^{nd} thoracic ganglionectomy on associated plantar and axillary hyperhidrosis merits evaluation as some patients obtain relief of plantar and axillary

hyperhidrosis following this surgical approach; mechanisms for these beneficial effects remain unclear at present.

Whereas the other indications for upper limb sympathectomy are atbest equivocal, primary hyperhidrosis is the one solid and universally acceptable indication for sympathectomy. With the large number of sympathectomies currently being undertaken for palmar hyperhidrosis and the greater public and clinical awareness of its treatment by minimal access surgery, an opportunity is presented to reappraise the role of the sympathetic nervous system in surgical practice.

2.2.1.2 CHRONIC REGIONAL PAIN SYNDROME (CRPS)

In 1854 Weir Mitchell first described the syndrome of causalgia during the American Civil War. Since then the term causalgia has been redefined several times. The term Complex Regional Pain Syndrome (CRPS) is currently used to describe the constellation of symptoms previously described as Causalgia, Reflex Sympathetic Dystrophy, Sudeck's Atrophy or, mimo-causalgia, amongst others.

The International Association for the Study of Pain (IASP) classification of the chronic regional pain syndromes (CRPS Types I and II) affords the early clinical recognition of this condition, and provides clearer definitions. The 4 diagnostic criteria (3 of which must be present to confirm the diagnosis) for CRPS Type I (previously Reflex Sympathetic Dystrophy) are: (Stanton-Hicks et al., 1995, Boas 1996).

1. the presence of an initiating noxious event or a cause of immobilization
2. continuous pain (disproportionate to an inciting event), allodynia or hyperalgesia
3. oedema, changes in skin blood flow or sudomotor activity in the region of pain
4. exclusion of conditions that would otherwise account for the degree of pain

CRPS type II has a peripheral nerve injury as the initiating factor together with criteria 2 – 4 as described for CRPS Type I.

The traditional therapeutic approach to CRPS is a conservative one. With respect to the upper limb, surgical intervention by cervical sympathectomy is usually indicated when the condition becomes refractory to medical treatment, and is responsive to sympathetic blockade.

The pathogenesis of CRPS is poorly understood. Several theories have been proposed. Lewis (1942) suggested that pain-producing vasodilatory substances are released at the site of injury. Doupe et al (1944) proposed that cross-linkage occurred between sympathetic efferents and sensory afferents. Leriche (1913) felt that the pain was secondary to vasospasm. That no consensus exists with respect to the pathogenesis is reflected in the current therapy of CRPS. Interpretations of the mechanistic aspects and the therapeutic modalities have long been varied and contentious. Primary treatment is invariably effected by neurologists, anesthetists, physicians and belatedly by surgeons. Initial treatment is conservative, employing tricyclic anti-depressants (Prothiden®), membrane-stabilisers (Tegretol®, carbamazepine) or Gabapectin, a selective voltage gated Ca^{2+} channel blocker and non-steroidal anti-inflammatory drugs. This therapeutic schedule (which is subscribed to by the Pain Clinic at Addington Hospital, Durban) is conventionally administered for up to 2 months; patients undergo intensive physiotherapy during this period. Stellate ganglion blocks (SGB) are performed if there is no clinical improvement. SGB may even prove to be curative in itself when the pain relief extends beyond the durations of the block. The guidelines for repeated SGB, when pain is not adequately controlled, are unclear. It has been recommended that if relief from repeated SGB becomes less effective or static, and if the initial response is dramatic but of a short duration, surgical sympathectomy should be undertaken (Mockus, 1987).

Two issues merit consideration. Firstly, successful SGB does require a measure of expertise. If an accurate block is to be obtained, the 1st thoracic ganglion component of the stellate ganglion- which subserves the upper limb- needs to be blocked.

Secondly, repeated SGBs may predispose to inflammation and scarring in the region of the stellate ganglion and the proximal sympathetic chain. This may make technically difficult any future procedure undertaken in this region.

The role of sympathectomy in the management of CRPS is not without criticism. It is argued that reports advocating sympathectomy are largely subjective and descriptive. There are no controlled randomized studies that have supported the use of sympathetic block or sympathectomy over placebo controls or pharmacological measures. Furthermore, the overall sympathetic outflow to the skin of the patient with CRPS, although often thought to be hyperactive, is normal when assessed by microneurography. Indeed sympathetic hypofunction is suggested by the low venous plasma concentrations of nor-adrenaline and its intra-neuronal metabolite 3,4 dihydroxyphenylethyleneglycol, from the painful area (Schott, 1995). Yet sympathetic denervation has been reported to be effective.

The rationale for sympathetic ganglionectomy, the timing of this approach and the accuracy of SGB in the management of CRPS merits review.

2.2.1.3 RAYNAUD'S DISEASE

This condition rarely progresses to severe finger ischaemia or gangrene. The natural history is characterized by periods of symptoms interspersed with periods of improvement, even remission. Sympathectomy was commonly performed in the past to treat patients with Raynaud's disease. Given the often transient relief obtained by sympathectomy, the availability of effective pharmaco-therapy and the tendency of even severe manifestations to resolve spontaneously, it is not surprising that in current practice sympathectomy is not widely recommended.

2.2.1.4 PERIPHERAL VASCULAR DISEASE

In the context of vascular disorders, sympathectomy largely holds an adjunctive status; it is therefore often suggested as salvage therapy. This is not surprising given the non-enduring effect of sympathectomy on the vasculature and the current status of reconstructive vascular surgery. It has been suggested that sympathectomy may be a useful adjunct in cases of critical ischaemia that need by-pass surgery. Advocates of this propose that minimal dilatation of the distal run-off vessels should at least in theory, exert a positive influence on both graft patency and overall limb perfusion. However, it is difficult to access the relative contributions played by by-pass surgery and sympathectomy.

In those patients with Buerger's Disease, the complete and permanent avoidance of tobacco in any form forms the cornerstone of treatment of this condition. Vasodilatory drugs may be used during exacerbation of the disease. It has been suggested that

sympathectomy may afford a more enduring effect, increasing the flow of blood to the skin of involved extremities to prevent development of ischaemic lesions and expedite healing of ulcerative and gangrenous lesions if present.

2.2.2 ISSUES IN TECHNIQUE

2.2.2.1 OPEN SYMPATHECTOMY VERSUS THORACOSCOPIC SYPATHECTOMY

The apparent ease of patient recovery, sometimes technical ease and smaller cosmetically acceptable incisions has firmly ensconced the practice of minimal access surgery.

Although initially creating a major impact on abdominal operations, the improvements in video technology, illumination and fibre-optics- has prompted a major resuscitation of the thoracoscopic approach. Yet, despite its current status, the value of the thoracoscopic approach has not been compared against the traditional "open" approach.

The thoracoscopic approach is widely perceived as most appropriate, on account of its apparent technical ease, reproducibility, patient acceptance and safety. Paradoxically, a randomized trial comparing thoracoscopic surgery versus the open supraclavicular approach (Hashmonai, 1994) reported the open supraclavicular approach to be superior. This issue clearly merits a review.

In the light of the innumerable favourable reports that attest to the vaunted status of thoracoscopic sympathectomy, it would be impossible to obtain permission to undertake

a prospective randomized trial comparing open sympathectomy to thoracoscopic sympathectomy. In the light of justifiable ethical restraint a case controlled study evaluating thoracoscopic sympathectomy with the most recently performed open sympathectomy was undertaken.

2.2.2.2 ANAESTHESTIC CONSIDERATIONS : SINGLE LUMEN ENDOTRACHEAL INTUBATION VERSUS DOUBLE LUMEN ENDOBROCHIAL INTUBATION FOR THPORACOSCOPIC SYMPATHECTOMY

In current surgical practice the technique for thoracoscopic sympathectomy for upper limb sympathectomy, its safety and ease has made this operation a popular one for conditions such as palmar hyperhidrosis. The often unsatisfactory conservative therapeutic options has led to even more patients than ever before presenting for thoracoscopic sympathectomy. The ease of the surgical technique has been alluded to; to make the procedure universally applicable, it is imperative that the anaesthetic technique is equally safe, effective and reproducible in the hands of an anaesthetist with standard training and ability. In this regard, in addition to the choice of induction and anaesthetic maintenance agents, the choice of endotracheal *vs* endobronchial intubation is crucial.

The traditional approach has been to perform the surgery (under anaesthesia) using a DLEBT (Double Lumen Endobrochial Tube) and then selectively collapsing the lung on the side being operated upon (Jedeikin, 1992; Hartrey, 1994). The placement of the expensive DLEBT requires anesthetic expertise which is not often available; DLEBTs are also expensive (costing up to $80 US). The benefit of a total lung collapse afforded by DLEBT has to be weighted against these drawbacks. Also warranting consideration is the fact that the operating surgeon requires no more than 5cm apical pneumothorax to

undertake the procedure; a total lung collapse is therefore unnecessary. With partial lung collapse attained with a SLET (Single Lumen Endotracheal Tube), thoracoscopic sympathectomy can be safely undertaken (Lee et al., 1994). Benefits associated with SLET use include ease of placement and a substantial cost saving (SLET costs $8 US!). To date a randomized evaluation of DLEBT *vs* SLET has not been undertaken.

2.2.2.3 EXTENT OF GANGLIONECTOMY FOR UPPER LIMB SYMPATHETIC DENERVATION

Currently thoracoscopic sympathectomy is universally recognized as affording the most effective option in obtaining an enduring treatment of palmar hyperhidrosis (Moran and Brady, 1991; Byrne et al., 1990). The extent of the sympathectomy undertaken for upper limb hyperhidrosis is controversial and ranges from an isolated resection of the 2nd thoracic ganglion (Hederman, 1994) (T2 ganglionectomy) to an excision of the sympathetic chain from the 2^{nd} to 4^{th} thoracic ganglion (Kux, 1978; Weale 1980). The most devastating and unpleasant side-effect of a thoracic sympathectomy undertaken for Primary Hyperhidrosis is compensatory hyperhidrosis. This side effect is largely unpredictable but is more likely to follow an extensive sympathectomy (Shelley and Florence, 1960; O'Riordain et al., 1993). The debility imparted by compensatory hyperhidrosis may be so severe that patients are known to regret the procedure and with hindsight, would have accepted the original condition. Thus Lin (1998) has described the technique of clipping the sympathetic chain (without transection of the chain or its branches); if unpleasant compensatory hyperhidrosis is reported post-operatively, the clips are removed. In 5 patients undergoing removal of clips (within 5 weeks of the procedure), the original hyperhidrotic state (without compensatory hyperhidrosis) was noted to return within 6 weeks of clip removal. This approach awaits further evaluation.

In this study the efficacy of a limited thoracic ganglionectomy undertaken for palmar and axillary hyperhidrosis and the incidence of compensatory hyperhidrosis following this limited ganglionectomy was prospectively evaluated.

2.2.2.4 OUTCOME OF THORACOSCOPIC SYMPATHECTOMY : MECHANISMS FOR FAILURE

In the minimal access surgery era the procedure to effect upper limb sympathectomy is safe, easy and widely reproducible (Byrne 1990 ; Lin,1990). This has led, universally, to an increase in the numbers of upper limb sympathectomies being undertaken (Lee, 1994). Whilst the outcome to sympathectomy in current practice is invariably successful, persistent (pSA) or recurrent (rSA) sympathetic activity, after a seemingly successful procedure, has refocused on the causes of this phenomenon. Explanations have been varied and often tenuous; these include the possibility of an incomplete operation, failure to appreciate an alternate neural pathway (ANP) e.g. the nerve of Kuntz, sympathetic regeneration and the misidentification of the sympathetic chain at surgery [Kuntz, 1927 ; Singh et al., 1998] .

Experience with early and late sympathetic failure following an apparently successful sympathectomy was evaluated with a view to establishing the mechanisms that result in failure.

2.3 ANATOMICAL CONSIDERATIONS

> *"the sympathetic nervous system, though nicely diagrammed in the anatomical texts, has often been found by the surgeon to be apparently anomalous beyond all understanding in its devious origins and ramifications. This has been the case particularly with the upper extremities."*
>
> *Ray et al. (1943)*

2.3.1 ALTERNATE NEURAL PATHWAYS

The gross anatomy of the upper limb sympathetic outflow has been a consistent issue of anatomical interest, fuelled largely by its clinical relevance. It has been suggested that the spinal origins of the sympathetic nervous system reside between the 2nd to 5th thoracic spinal segments. The evidence for this is based on histological staining. Tenuous, however, are the definitions of the neural networks of the sympathetic upper limb outflow. Thus, the mapping of sympathetic neural outflow from the spinal cord is structured on clinical extrapolation, surgical hindsight and complications to surgical endeavour (eg. the development of a Horner's Syndrome following stellate ganglionectomy). Whereas there have been advances in the understanding of the physiology of the sympathetic nervous system and the indications for sympathectomy, the anatomy of the sympathetic nervous system and its teachings has remained as outlined as at the turn of the last century (Figure 4).

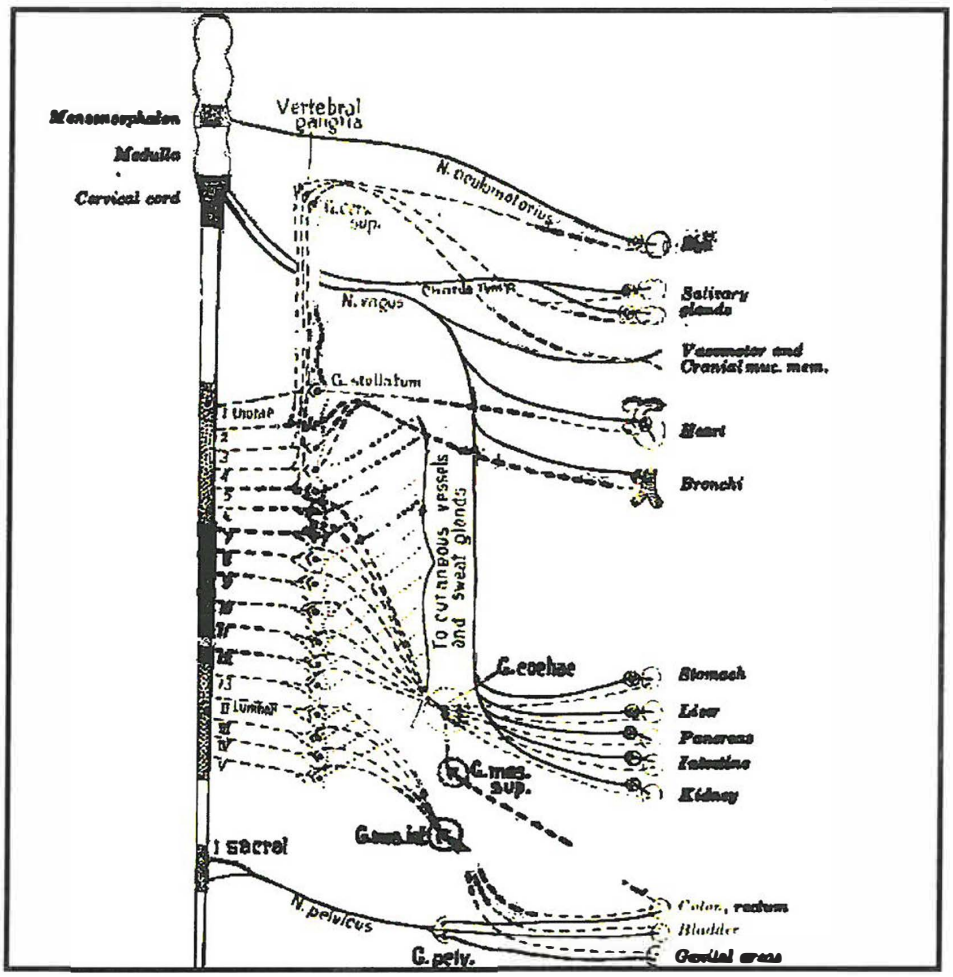


Figure 4 : Schematic diagram of the autonomic nervous system.

——— cranial and sacral outflow (parasympathetic)

..... thoraco-lumbar outflow (sympathetic)

(Adapted from Kuntz, 1934)

Current clinical experience suggests that the 2nd thoracic ganglion is pivotal to the upper limb sympathetic outflow. It is therefore appropriate that the gross anatomy and neural pathways pertinent to the 2nd thoracic ganglion be fully appreciated. Anatomical variations in the sympathetic nervous system were traditionally credited for instances of operative failure following attempts at upper limb sympathectomy.

Sympathectomy as a valid surgical procedure was incorporated into surgical practice during the 1920s to 1930s. The standard surgical approach was a stellate (fused inferior cervical and T1 ganglia) ganglionectomy. Whilst this approach produced an upper limb sympathectomy effect consistently, it also left the patient with a Horner's Syndrome. This complication may have been an acceptable complication during that era and was sometimes addressed by performing a contra-lateral stellatectomy to make the effect more acceptable. Recurrent or persistent sympathetic activity following stellate ganglionectomy was a vexed issue and was attributed to nerve regeneration or alternate neural pathways, for example, the nerve of Kuntz. Notwithstanding its outcome, stellate ganglionectomy did contribute to formulating our understanding of the sympathetic outflow of the proximal sympathetic chain.

Given that the highest spinal outflow to the sympathetic chain is to the 1st thoracic ganglion; the following may be extrapolated :

i. the origin of the sympathetic supply to the eyelid has to be via the 1st thoracic root, the source of the highest sympathetic spinal outflow (Figure 2)

ii. effective upper limb sympathectomy by 2nd thoracic ganglionectomy would suggest that the 1st thoracic and inferior cervical ganglia are not pivotal to upper limb sympathetic supply; these ganglia (2nd thoracic)

may represent either a post-ganglionic (to the 2nd thoracic ganglion) component or a more downstream component of the pre-ganglionic sympathetic outflow to the upper limb. With the successful outcome to the 2nd thoracic ganglionectomy (and minimal sequalae) it is a moot point whether defining this as a pre- or post ganglionic section is necessary or worthy of investigation.

During the era of stellate ganglionectomy anatomists focussed on the variations of sympathetic neural outflow to define the causes of persistent or recurrent sympathetic activity. Up to then anatomical research focussed on the spinal origins of the sympathetic nervous system, an approach hamstrung by inappropriate staining technique, inadequate magnification and little clinical experience. The clinical despair prompted by persistent sympathetic activity following stellate ganglionectomy led to the performance of more extensive ganglionectomies; thus surgery either included or excluded the stellate ganglion in addition to removing various segments of the sympathetic chain (2nd to 5th thoracic ganglia).

Albert Kuntz, a renowned neuroanatomist of St Louis University School of Medicine (USA), drew attention in 1927 to a variable intrathoracic ramus (ITR) between the 2nd intercostal nerve and the ventral ramus of the 1st thoracic nerve, proximal to the pointwhere the latter gave a large branch to the brachial plexus (Figure 5). This 'ramus' was located in front of the neck of the 2nd rib in the thorax. This nerve, called the nerve of Kuntz, was reported by Kuntz himself to be present in up to 53% of cadaveric dissections.

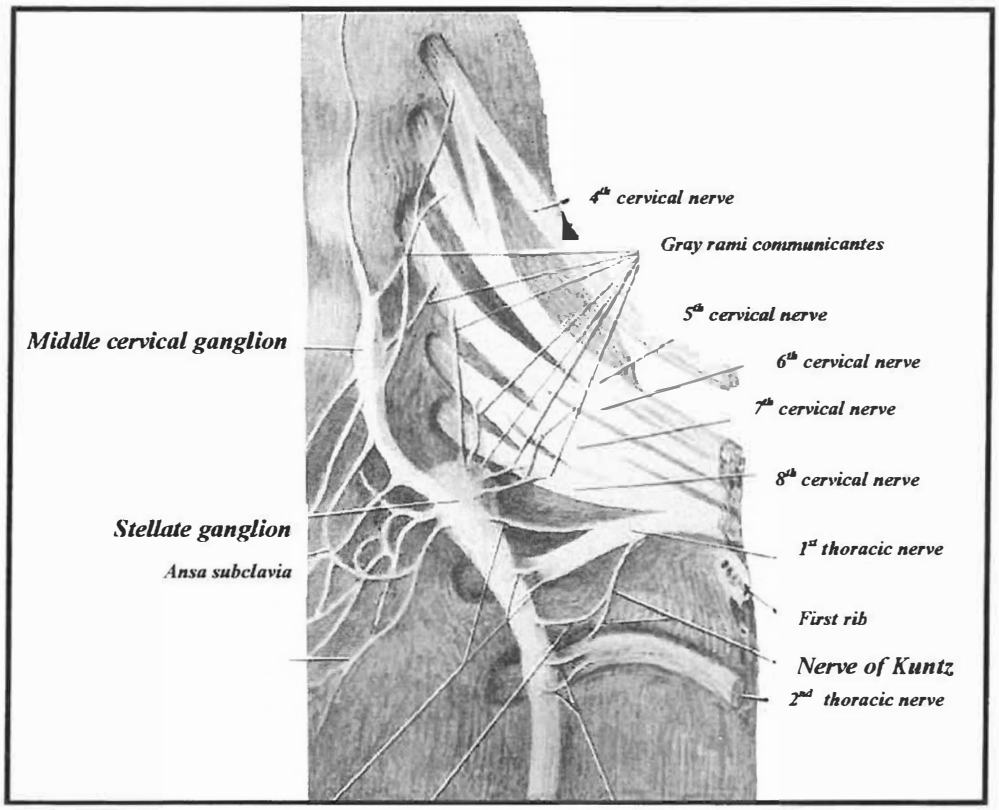


Figure 5 : *Drawing from the cadaver to illustrate the inconsistent intrathoracic ramus from the 2nd to the 1st thoracic nerve and the communicating rami joining the brachial plexus (Adapted from Kuntz, 1934)*

The clinical significance of the nerve of Kuntz resides in the supposition that following a stellate ganglionectomy sympathetic outflow from the spinal cord may pass to the 2nd thoracic root and then , via the nerve of Kuntz , to the periphery via the 1st thoracic nerve root (Figure 6).

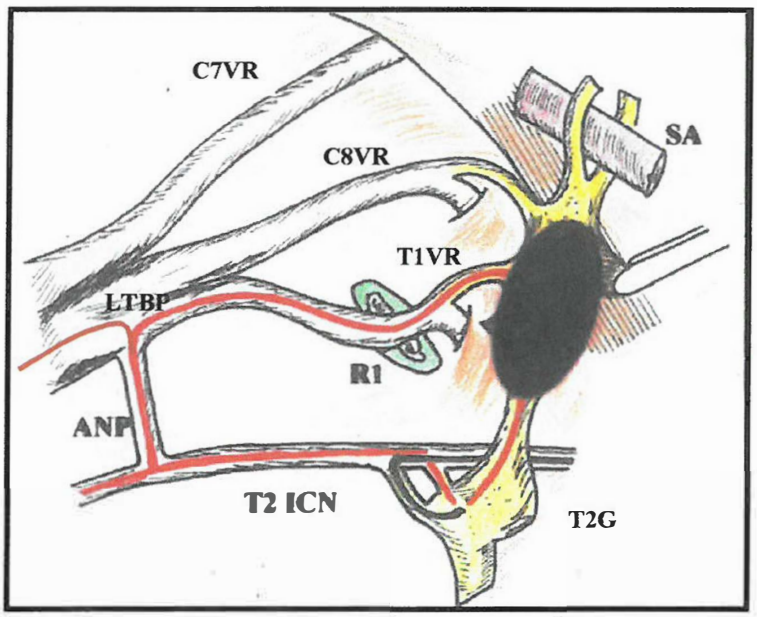


Figure 6 : *The neural pathway to the brachial plexus is not interrupted by stellate ganglionectomy when an alternate neural pathway is present*

C7, C8, T1 VR	-	7th, 8th cervical; 1st thoracic ventral rami
SA	-	Subclavian artery
T2G	-	2nd thoracic ganglion
LTBP	-	Lower trunk of brachial plexus
T2ICN	-	2nd intercostal nerve
ANP	-	Alternate neural pathway
R1	-	1st rib

Further descriptions of the nerve of Kuntz were noted (Table 5, Figure 7) : a grey ramus from T2 ganglion or the sympathetic trunk was traced directly into the ramus connecting the 1st and 2nd thoracic nerves. In other cases, a ramus from the SG was traced into the ramus described above (Kuntz, 1927; Jit and Mukerjee, 1960). Jit and Mukerjee (1960) noted an incidence of 30% of a ramus between the SG and the 2nd

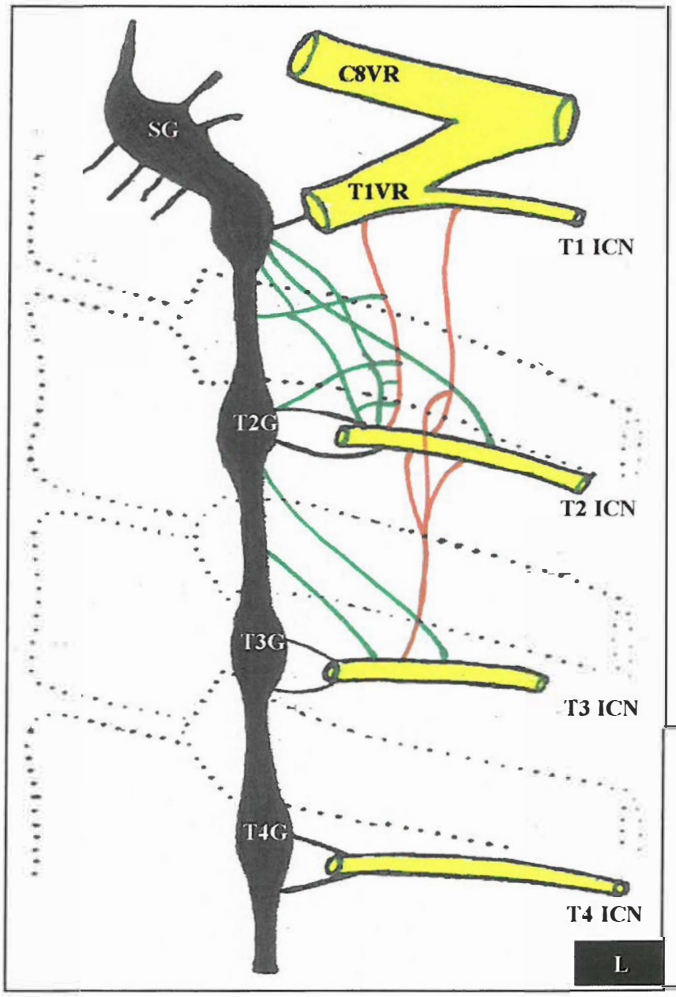
intercostal nerve, irrespective of whether the nerve of Kuntz was present or not. These descriptions kindled an interest in defining other neural pathways, not only in relation to the 1st and 2nd thoracic nerves but to the 3rd and 4th intercostal nerves as well.

In subsequent studies by Kirgis (1941), Kirgis and Kuntz (1942) and Kuntz (1946), a similar 'ramus' joined the 2nd and 3rd intercostal nerves in front of the 3rd rib. Kirgis and Kuntz (1942) recorded an incidence of 54.5% of this ramus in their series of 88 dissections. This ramus can divide into two branches to join the 2nd intercostal nerve at more than one place. Communicating rami were also reported from the 3rd intercostal nerve to the 2nd thoracic ganglion and to the sympathetic trunk just below the 2nd thoracic ganglion. Jit and Mukerjee (1960) recorded the presence of a 3rd communication between the 3rd and 4th intercostal nerves.

Kirgis (1941) depicted a recurrent ramus from the 3rd intercostal nerve which joined either the 2nd thoracic ganglion or the sympathetic trunk just inferior to it. This recurrent ramus arose either from the grey communicating ramus of the 3rd intercostal nerve or from the nerve just distal to the point at which it was joined by the grey ramus. The recurrent ramus also joined the 2nd intercostal nerve or its grey communicating ramus. This ramus constitutes an alternate neural pathway through which fibres emerging from the sympathetic trunk via the grey ramus of the 3rd intercostal nerve may reach the 2nd intercostal nerve, from which they enter the brachial plexus via the ITR between the 2nd intercostal nerve and the ventral ramus of the 1st. To date, none of these variants have been classified in terms of their anatomical or clinical relevance. This lack of clarity with respect to the spectrum of variations merits a re-consideration given the vast increase of sympathectomies undertaken at present.

TABLE 5 : INCIDENCE OF NERVE OF KUNTZ

REFERENCE	SAMPLE SIZE	INCIDENCE (%)
Kuntz (1927)	96	51 (53.1)
Kirgis (1941)	25	18 (72)
Kirgis and Kuntz (1942)	88	66 (75)
Jit & Mukerjee (1960)	100	38 (38)
Groen et al (1987)	6	4 (66.7)



SG	-	Stellate ganglion
C8,T1VR	-	8th cervical; 1st thoracic ventral rami
T2,3,4G	-	2nd,3rd,4th thoracic ganglion
T1,2,3,4 ICN	-	1st, 2nd, 3rd, 4th intercostal nerves

***Figure** 7 : Alternate neural connections described by Kuntz (1927) and Kirgis and Kuntz (1942)*

These variations were collectively and perhaps inappropriately also described as the nerve of Kuntz. The clinical implications of the distal alternate neural pathways on upper limb sympathetic supply are essentially negligible and therefore have not engendered anatomical interest. For practical purposes it is the variations located in the 2nd intercostal space – between the 1st and 2nd thoracic roots that are of surgical significance with respect to upper limb sympathetic supply.

The current practice of an isolated 2nd thoracic ganglionectomy – a procedure that does not attempt to define the nerve of Kuntz – is consistently associated with a successful upper limb sympathectomy. Given the long held view that alternate neural pathways such as the nerve of Kuntz may serve as conduits for upper limb sympathetic supply , the significance of alternate neural pathways in current surgical practice merits review.

The proximity of alternate neural pathways to the sympathetic chain also merits evaluation; whilst the isolated 2nd thoracic ganglionectomy is predictably successful, it may be conceivable that alternate neural pathways are transacted inadvertently during this technique. This would be possible when the alternate neural pathways are closely adjacent to the sympathetic chain. A truly isolated 2nd thoracic ganglionectomy will then relegate the significance of alternate neural pathways.

Since the 2nd thoracic ganglion is pivotal to upper limb sympathectomy, it is crucial that it is correctly identified i.e not misinterpreted as is conceivable when the 2nd ganglion is fused to the 1st thoracic or stellate ganglia. Misinterpretation of the 2nd thoracic ganglion may also result when the stellate ganglion is not fused and the lower component (the thoracic component) extends over the neck of the 2nd rib to beyond its lower border. Appreciation of the location of the 2nd thoracic and stellate ganglia will

therefore be of surgical relevance. In this context, acquaintance with the shape and dimensions of the stellate ganglion may be valuable; likewise knowledge of the location of the 2nd thoracic ganglion in the 2nd intercostal space and the spectrum of rami communicantes associated with it will be of value to the operating surgeon.

2.3.2 STELLATE GANGLION BLOCK : AN ANATOMICAL RE-APPRAISAL

The role of the so-called Stellate Ganglion Block (SGB) in the diagnosis, determination of prognosis and management of Chronic Regional Pain Syndrome (CRPS) has been shown in the clinical component of this study, to be unpredictable. The SGB has long been considered pivotal in defining those patients who may benefit from a sympathectomy; thus, an inaccurate SGB will mislead the clinician and may deny a patient a potentially beneficial procedure. A successful (or positive) SGB in the context of CRPS is defined in our practice as the development of a transient Horner's Syndrome [with even minor, evanescent eye signs] with the alleviation of the upper limb pain of CRPS. This latter effect is described as being reflective of Sympathetic Maintained Pain (SMP); in such a situation a sympathectomy would be invaluable in the management of CRPS.

The accuracy of SGB in effecting an isolated upper limb sympathetic block (and thereby diagnosing SMP) is unknown. Furthermore, blockade of the sympathetic ganglia /and chain in the cervical and upper thoracic region is incorrectly referred to as SGB. The location, shape and extent of the proximal sympathetic chain and ganglia are known to be varied ; the stellate ganglion itself is present in up to 80% of the population

(Jit and Mukerjee, 1960). To effect a complete upper limb sympathetic blockade, it is clear, from current surgical experience that this may occur without the development of a Horner's Syndrome; this is reflected in the surgical outcome to a 2nd thoracic ganglionectomy. Thus, a more accurate description is either a lower cervical sympathetic block or upper thoracic sympathetic block (cervico-thoracic sympathetic trunk block) (Elias, 2000a,b).

An accurate definition of upper limb SMP mandates the isolated blockade of the upper limb sympathetic pathway. In practical terms this presently may not be possible. Multiple approaches have been used to localize the lower cervical sympathetic ganglia and the stellate ganglion. This, in itself, represents a failure to appreciate that the sympathetic pathway to the upper limb is effectively independent of the stellate ganglion. In our practice, the traditional approach to effect an upper limb sympathetic blockade is a 'blind' technique i.e not using ultrasound, MRI or fluoroscopy for the localization of the sympathetic chain.

Several 'blind' techniques have been described. These include the paratracheal approach (Moore, 1954), the anterior approach, the lateral approach, the posterior approach and the tissue displacement method (Atkinson, 1982). Arguably, the most widely used of these is the paratracheal approach; it is the technique favoured in our Pain Clinic. The precise point of the injection in this technique varies between the C6 and C7 vertebral level; classically, the needle is recommended to be perpendicular to the skin surface at the chosen landmark. In an anatomical study using the anterior "standard" technique, the injectate was noted to spread onto the posterior mediastinum and over the pleura; there was no spread onto the thoracic sympathetic chain

(Guntamukkala and Hardy, 1991). Hogan (1992) reported the spread of the local anaesthetic to be anterior to the position of the stellate/cervical sympathetic ganglia. It is suggested that it is the unpredictable nature of the local anaesthetic extravasation that may account for the unreliable predictive value of the so-called SGB. In order to obtain a predictable blockade of the stellate/cervical sympathetic ganglia and the proximal thoracic chain, a modified anterior technique was evaluated.

2.4 PATHOLOGICAL CONSIDERATIONS

A limited excision of the 2nd thoracic ganglionectomy for primary palmar hyperhidrosis is well established as the prime indication for sympathectomy. The role of this procedure in other conditions is controversial (eg. vascular disorders). Sympathectomy is, however, gaining acceptance as valid therapy for Chronic Regional Pain Syndrome (CRPS) and cases of Raynaud's phenomenon not responding to medical therapy.

Notwithstanding the invariably excellent outcome to sympathetic ganglionectomy for primary palmar hyperhidrosis and, on occasions, for CRPS, the role of the sympathetic nervous system in the pathogenesis of these conditions has not been evaluated. The reasons for this are principally 2 fold:

i) in many surgical practices the sympathetic ganglia are coagulated and thereby not presented for histological evaluation.

ii) the rationale for the histological evaluation of excised ganglia is invariably to

confirm a sympathectomy, particularly when technical difficulty was encountered during surgery. The histo-pathologist particularly seeks the presence of sympathetic ganglia rather than subtle pathological changes.

Our experience with routine histological (Haematoxcylin and Eosin staining) evaluation of sympathetic ganglia excised from patients with hyperhidrosis and CRPS have demonstrated an infiltration of inflammatory cells with occasional fibrosis. The normal histological profile of sympathetic ganglia shows an absence of cellular infiltrations. The significance of the described cellular infiltrate in the pathogenesis of hyperhidrosis and CRPS has not been previously considered. In addition, evaluation of the sympathetic ganglia has not been pursued as these are thought to interrupt the pathological process rather than to mediate it, as proposed by currently accepted postulates.

a) Primary Hyperhidrosis

There are 2 types of sweats glands, eccrine and apocrine. The human skin contains approximately 2 million eccrine sweat glands (Bisbal et al, 1987). The production of sweat depends on the functional innervation of eccrine sweat glands by intact non-myelinated C fibres of sympathetic nerves. Glands deprived of their post-ganglionic nerve supply cease to respond to any stimuli, even though they remain histologically normal. The eccrine glands are present over the entire body surface, but are most numerous on the palms, soles and, to a lesser extent, on the back and chest (Cunliffe et al., 1976) Apocrine glands are confined to the axilla, the areola of the nipple, the

anogenital area and the external auditory meatus. The sweat produced by these glands is usually in small quantities and has little role to play in hyperhidrosis. Apocrine glands also have no direct secretory innervation, although local stimulation with epinephrine will result in sweat production (Leung et al., 1999).

Whereas there has been considerable research into the pathogenesis of CRPS this is not so for primary hyperhidrosis. The cause of hyperhidrosis remains obscure; indeed the cause is considered to be of no clinical significance since there is no known association of primary hyperhidrosis with any medical condition. This contrasts with the situation wherein hyperhidrosis may be associated with thyrotoxicosis and phaechromocytoma, conditions that prompt wide investigations, treatment and follow-up because of their formidable physiologic and clinical impact. Since there is considerable knowledge of the sweat gland distribution and its innervation it is not surprising that hitherto interest has focused on the sweat gland morphology. In primary hyperhidrosis, the sweat glands of the palms and soles are normal in histology and numbers. The sympathetic nerve supply to these areas is also normal (Ellis, 1975 and Leung, 1999).

b) Chronic Regional Pain Syndrome

That various mechanisms have been suggested for the evolution and progression of CRPS underscores the current failure to crystallize the pathogenesis of this condition. The hard evidence for these mechanisms are invariably lacking. An evaluation of the injured nerve- the provocative factor for the condition - is invariably not feasible; likewise the evaluation of the affected skin or muscle is neither practical nor ethical. There is, however, strong clinical evidence for an underlying sympathetic over activity

viz altered skin colour, hyperhidrosis, temperature change, piloerection and swelling (Hannington-Kiff, 1994). Furthermore a favourable outcome to sympathectomy has been reported in patients with CRPS (Abu-Rahma, 1994; Mockus, 1987; Olcott et al., 1991). Clinicians have long observed that patients suffering from CRPS may have the pain associated with these conditions as dependant on activity in the sympathetic nervous system; this is often referred to as "sympathetically maintained pain". It has been demonstrated that an abnormal contact develops between the sympathetic nervous system and the sensory nervous system following peripheral nerve injury, prompting an enhanced sensitivity to catecholamines (Janig et al, 1996).

Several sites of coupling between sensory and sympathetic nervous system have been proposed and tested in animal models (Perl et al, 1992, Levine et al, 1994 and Blumberg 1982). The possibility of direct coupling between the sympathetic and sensory nervous systems in the dorsal root ganglion (DRG) has received much attention with numerous studies demonstrating that peripheral nerve injury leads to sympathetic axons sprouting into the DRG has been described following the experimental ligation of the sciatic nerve (McLachlan et al., 1993).

The mechanisms for the onset of the sympathetic sprouting are unclear. It is likely that neurotrophic factors and cytokines may be crucial to the process. The cytokine Leukaemia Inhibitory Factor (LIF) has been demonstrated to stimulate sympathetic sprouting (Thomson et al., 1998). The neurotrophin Nerve Growth Factor (NGF) has also been demonstrated to induce sympathetic sprouting in the DRG (Isaacson et al, 1992 and Jones et al, 1999). The terminals of the sprouted neurons have been shown to

form functional synapse-like structures with the cell bodies (McLachlan et al., 1993). These structures could be involved in the formation and maintenance of abnormal excitation arising from DRG, a hypothesis supported by electrophysiological studies in which sympathetic stimulation increased sensory ectopic discharge from the DRG (Devor et al, 1994). The time scale of sprouting corresponds to the onset of allodynia and hyperalgesia, the hallmarks of sympathetic maintained pain. Whilst the information regarding changes has been substantiated in other studies, what prompts this development remains obscure. There is evidence that pain is mediated peripherally as well as centrally by cytokines; hence the common failure of peripherally acting analgesics to control pain. The retrieve of the cellular infiltrate, particularly the lymphocytic infiltrate, in the sympathetic ganglia from patients with CRPS may provide further insight into the possible pathological process of this conditions. The role of the sympathetic nervous system - either in concert or sequential to the DRG pathology has not been previously considered. The precise role of the immunological system vis-a-vis the sympathetic ganglia in the pathophysiology of CRPS has not been evaluated.

In the light of foregoing information, an investigation into the nature of the inflammatory infiltrate in the ganglia of excised from patients with Primary hyperhidrosis and CRPS is appropriate. The definition of these lymphocyte populations being B-type or T-type (helper or suppressor) may provide insight into the pathogenesis of these conditions.

CHAPTER 3

MATERIALS AND METHODS

3.1 CLINICAL COMPONENT

A prospective evaluation of all patients referred for and under-going upper limb sympathectomy for

i. Primary hyperhidrosis

ii. Chronic Regional Pain Syndrome

iii. Raynaud's Disease

iv. Peripheral Vascular Disease

SETTING

The three academic hospitals that serve as referral centres with catchment areas geographically and socio-economically distributed throughout the Durban Function Region [in the province of Kwa-Zulu Natal, South Africa]. In addition to these academic hospitals (King Edward VIII, R.K. Khan and Addington Hospitals), two private hospitals (City and Chatsmed Garden Hospitals) with comparable surgical services also served as a setting for the study.

Patients were interviewed, assessed, treated and reviewed at the respective presenting hospitals.

3.1.1 PRIMARY HYPERHIDROSIS

Patients presenting with debilitating palmar hyperhidrosis- sweating in amounts that is greater than that required for insensible loss or physiological needs- were considered. The degree of hyperhidrosis was considered to be debilitating when it had affected schoolwork (smudging of writing, slipping of computer keyboard), was socially embarrassing (leading to social withdrawal or low self esteem) or if it affected vocation (switchboard or computer operator, use of fine hand instruments).

Exclusion Criteria :

- Patients were excluded if there was an underlying cause for the hyperhidrosis.
- If the hyperhidrosis was considered to be generalized (rather than isolated to the palms with associated axilla or plantar sweating).
- Patients with isolated plantar or axillary hyperhidrosis.

The severity of the hyperhidrosis as well as the outcome to surgery was scored on a linear analogue scale (LAS) from 0-10. The score of zero represented complete anhidrosis or complete satisfaction; the score of 10 represented dripping hyperhidrosis or total dissatisfaction with the outcome. The spectrum of the presenting hyperhidrosis was further categorized as being mild (1-3), moderate (4-6) or severe (7-10). Likewise the outcome to operation was quantified as being excellent (1-3), satisfactory (4-6) or poor (7-10).

The biographic data collected included the age, onset and duration of symptoms, sex and race.

The distribution pattern of the hyperhidrosis was documented i.e palmar and/or axillary and/or plantar hyperhidrosis. If excessive sweating was present in more than one region, patients would be asked to prioritize the most debilitating of these regions.

The possible side effects of upper limb sympathectomy to treat hyperhidrosis were fully explained to the patients. In particular, the possibility of excessive sweating developing along the trunks, back and thighs (compensatory hyperhidrosis) was emphasized. Other effects (such as Horner's Syndrome) though remote, were also mentioned.

Thoracoscopic sympathectomy was the favoured approach for the upper limb sympathectomy. In patients suspected of having pleural adhesions (following previous thoracotomy, lung trauma or chronic lung disease eg. pulmonary tuberculosis, thoracoscopic approach would be attempted, notwithstanding the difficulty of attaining an adequate lung collapse to undertake an adequate thoracoscopy. If pleural adhesions were suspected pre-operatively, the patients would be given the option of undergoing the 'open' operation. The 'open' procedure undertaken will be the supraclavicular (described by Telford, 1935).

- Following surgery, patients were reviewed at one week and then at one month following the procedure. The effectiveness of the sympathectomy on palmar hyperhidrosis was evaluated. In a subset of patients presenting with palmar

hyperhidrosis, the effect on associated axillary and plantar hyperhidrosis was evaluated. Subsequent review at three month intervals would be undertaken by telephonic interviews.

3.1.2 CHRONIC REGIONAL PAIN SYNDROME

Patients were assessed at the Pain Clinic at Addington Hospital; anesthetists, psychologists, physiotherapists and occupational therapists were involved in the evaluation and initial therapy. Only patients with CRPS (Type II) were evaluated. Details of the precipitating injury were documented. The duration of the pain (in months), details of therapy used until referral for sympathectomy were noted. The number of stellate ganglion blocks performed, and the outcome for these were noted. The pre-operative degree of pain was evaluated by a visual Linear Analogue Scale from 0 to 10, 10 being the worst degree and 0, no pain.

Criteria for inclusion

i. Adequate and complete treatment of the precipitating injury [debride event, fracture mobilization, repair of associated soft tissue injury (including nerve injury) and treatment of any infection].

ii. Syndrome follows a nerve injury.

iii. Spontaneous pain, allodymia, hyperalgesia, not necessarily limited to the territory of the injured nerve.

iv. There is or has been evidence of edema, skin blood flow abnormality or abnormal sudomotor activity in the region of the pain since the inciting event.

Criteria for exclusion

i. Excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.

ii. The inability to localize the underlying nerve injury.

The initial assessment was undertaken at the Pain Clinic at Addington Hospital. The diagnosis was made entirely on clinical assessment. Standard biographic data (age and sex) was collected.

Initial treatment was pharmacological and included :

- Tricyclic anti-depressant (Prothiaden®)
- Membrane stabilizers (Tegretol® or Gabapectin, a selective voltage gated Ca^{2+} channel blocker)
- Non-steroidal anti-inflammatory agent

With the pharmacotherapy, regular active physiotherapy was instituted.

Unsatisfactory clinical progress on the outlined therapeutic schedule prompted the use of a Stellate Ganglion Block (SGB). The SGB was performed by a specialist anesthetist under local anesthesia via the supraclavicular paratracheal approach. With the patient supine and the neck extended to the contralateral side, the stellate ganglion was localized along the medial aspect of the sternocleidomastoid muscle at the level of the cricoid cartilage. The needle is advanced posteriorly between the carotid and internal jugular sheaths, aiming for the lateral bony mass of the C7 and T1 vertebrae. 10ml of local anesthetic (0.25%

Bupivacaine solution) was then injected. Classically, development of a Horner's Syndrome with warming and drying of the hand and relief of pain indicated a successful SGB.

When symptoms recurred after an initially satisfactory response to SGB, the block was repeated. Patients were offered sympathectomy when the clinical progress was unsatisfactory, notwithstanding repeated SGB. Prior to sympathectomy, the number of SGBs performed was documented. The duration of symptoms until performance of sympathectomy was noted. The degree of pain was independently assessed by using a Linear Analogue Scale (LAS); using a 1cm graduated line; patients were asked to quantify their pain from 0 (no pain) to 10 (worst, most unbearable pain). Following sympathectomy, outcome to surgery were also assessed on a LAS, independently. The patients progress were monitored at the one week and one month review (at the Outpatient's Department). Longer review, if necessary, was effected telephonically.

3.2 ISSUES IN TECHNIQUE

THORACOSCOPIC SYMPATHECTOMY

Informed consent was obtained in patients evaluated as being suitable for upper limb sympathectomy. The thorascopic approach was always attempted. When the thorascopic route was not feasible (because of technical or anatomical factors such as pleural adhesions or pleural thickening) in patients with CRPS an open sympathectomy was undertaken under the same anaesthetic. This surgical attitude is reflective of the progressively debilitating effect of CRPS.

By contrast, if thorascopic sympathectomy was not feasible in patients with hyperhidrosis recourse to the open approach was dependant on the options given to the patient pre-operatively. Anatomical factors that precluded the thorascopic approach because of pleural adhesions was suspected in patients with previously treated chronic lung disease, previous thoracotomy or lung trauma.

Surgeons performing thorascopic sympathectomy were technically proficient and had participated in a basic minimal access surgical skills course. A thorough understanding of the anatomy of the sympathetic chain, its variations, landmarks and relation to adjacent structures was mandatory. When procedures were performed by surgical trainees, these procedures were overseen by an experienced surgeon facile with the procedure. Because there are no universally accepted criteria for what constitutes a surgeon experienced in thorascopic surgery; it was considered that the performance of at least 30 procedures satisfied this requirement.

Surgeons performing thorascopic surgery were familiar with the open sympathectomy approach since this maybe necessary to effect sympathectomy.

Pre-operative Assessment

All patients had an evaluation of their full blood count, urea and electrolytes and blood glucose to ascertain their fitness for a general anaesthetic; however, in younger patients(less than 18 years) only the haemoglobin was evaluated.

If there was co-existent cardio-pulmonary disease, a chest x-ray and electrocardiograph was done.

Technique

I. Thoracoscopic sympathectomy: Because it is the preferred approach it is described in detail. Depending on their accessibility to the hospital, patients were admitted on the morning of the procedure, having being fasted from 18:00hrs the previous evening.

The procedure was performed under a standardized general anesthetic. Intra-operative analgesia was provided by Sufenta® and Marcaine® with infiltration to the proposed port sites. A single lumen endotracheal tube was routinely used, apart from a group in whom the double lumen endotracheal tube was evaluated. A non-steroid anti-inflammatory suppository was inserted following induction of the anesthetic.

Intra-operative monitoring included continuous measurement of arterial blood pressure, pulse oximetry, end tidal carbon dioxide concentration, electro-cardiography and peak airway pressure.

The patients are placed in the supine position and in 30 degree reverse Trendelenberg position. A small pillow is located between the scapulae to throw the chest into profile. The drapes are placed from the clavicles to the xiphoid, as well as amply exposing the axilla. Depending on the prospect of converting to the open procedure, the supraclavicular region was also prepared for this possibility..

Mechanical ventilation was stopped, facilitating partial collapse of the lung. Simultaneously the ipsilateral pleural space was insufflated with carbon dioxide delivered via a Veress needle; the Veress needle was placed posterior to the lateral aspect of the pectoralis major muscle at the level of the sternal angle (Plate 1). The carbon dioxide insufflation was continued only if the lung apex obscured the dissecting field , to no more than an intra-pleural pressure of 7cms water. The patient's ventilation was maintained by intermittent shallow manual ventilation.

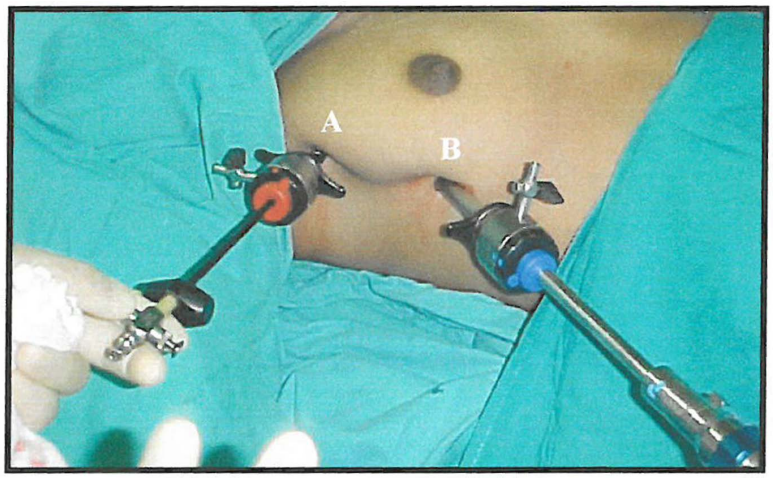


Plate 1 : *Port placement*

Dissection port (5mm) – [A] along the 3rd intercostal space posterior to pectoral fold

Camera port (5mm) – [B] along the anterior axillary line, 5th intercostal space

A 5mm port was then introduced along the 5th intercostal space in the anterior axillary line. Care was taken to ensure that the trocar is placed accurately, without impinging on the over-or underlying rib. Through this port a 5mm telescope (either 0 degrees or 30 degrees) connected to a video monitor was passed into the pleural space. Thoracoscopic evaluation of the pleural apex was conducted. Total lung collapse is unnecessary, an apical pneumothorax no more than 8cms being adequate to identify the relevant section of the

sympathetic chain. Continued pleural insufflation is not necessary. The telescope could be used to inferiorly displace lung obscuring adequate visualization of the chain; the telescope was also used to take down soft adhesion by blunt dissection.

At the site of the Veress needle a second 5mm point was placed. This port served as the access for the dissecting instrument. Accurate intercostal placement of the trocar – taking precaution to avoid bruising of the ribs - was essential (to obviate post-operative intercostal neuralgia).

A right angled hooked diathermy probe was used to identify the sympathetic chain which typically courses over the neck of the ribs. The important landmark is the 2nd rib; this was readily recognized as the most superiorly visible rib. The 1st rib, over the neck of which lies the stellate ganglion, is usually not seen. The stellate ganglion (mainly the inferior component) is not directly evident as it is covered by a characteristic yellow fat pad.

If the sympathetic chain was not readily seen overlying the neck of the 2nd rib, it was palpated by stroking the diathermy probe over the neck of the rib.

The pleural overlying the chain was then stripped from the inferior aspect of the 2nd rib upto the midportion of the 3rd rib. This was facilitated by initially creating a pleural window adjacent to the chain by using diathermy. The hook was then used to strip the pleura to expose the sympathetic chain up to the superior border of the 3rd rib..

The interganglionic component of sympathetic chain , between the stellate ganglion and the 2nd thoracic ganglion , was mobilized. It was usually free of neural connection. Thereafter, the interganlionic segment between the 2nd and 3rd thoracic ganglion was similarly mobilized. Bowstringing these two interganglionic segments brought the 2nd thoracic ganglion into profile. Gentle traction on this ganglion revealed its connections (white and grey rami communicantes) to the underlying intercostal nerve.

The connections were hooked and individually transected by cautery. Cautery (unipolar) was not used on the ganglion or its interganglionic connections; being unipolar it may inflict coagulative necrosis on the chain in an unpredictable manner. Injury to the intercostal artery which passes between the rami communicantes is easily avoided when the ganglion is mobilized in the manner outlined (Plates 2-8).

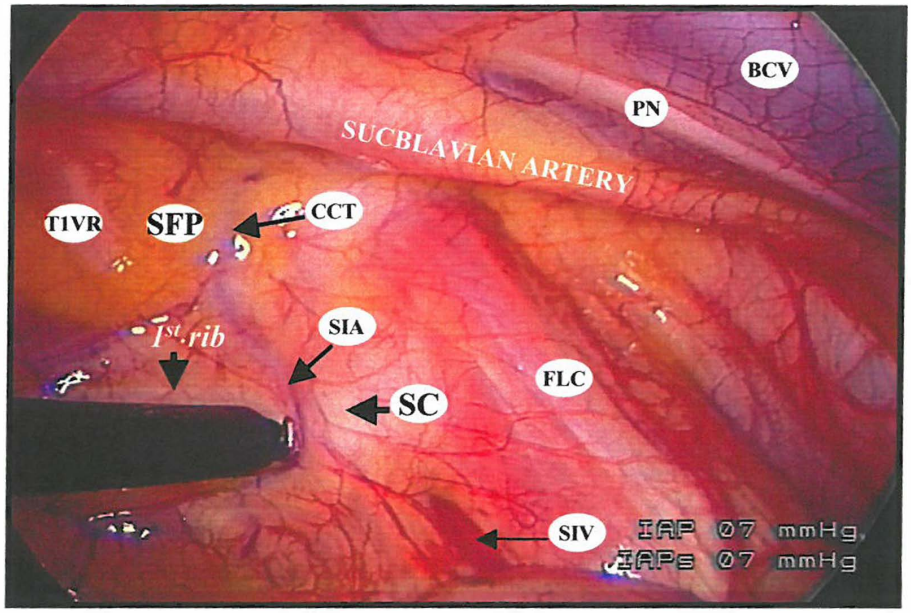


Plate 2 : *View at right thoracoscopic sympathectomy*

BCV -	Brachiocephalic vein	**SIA** -	Superior intercostal artery
PN -	Phrenic nerve	**SC** -	Sympathetic chain
T1VR-	T1 ventral ramus	**SIV** -	Supreme intercostal vein
SFP -	Stellate fat pad	**FLC** -	Fascia over longus colli muscle
CCT -	Costocervical trunk		

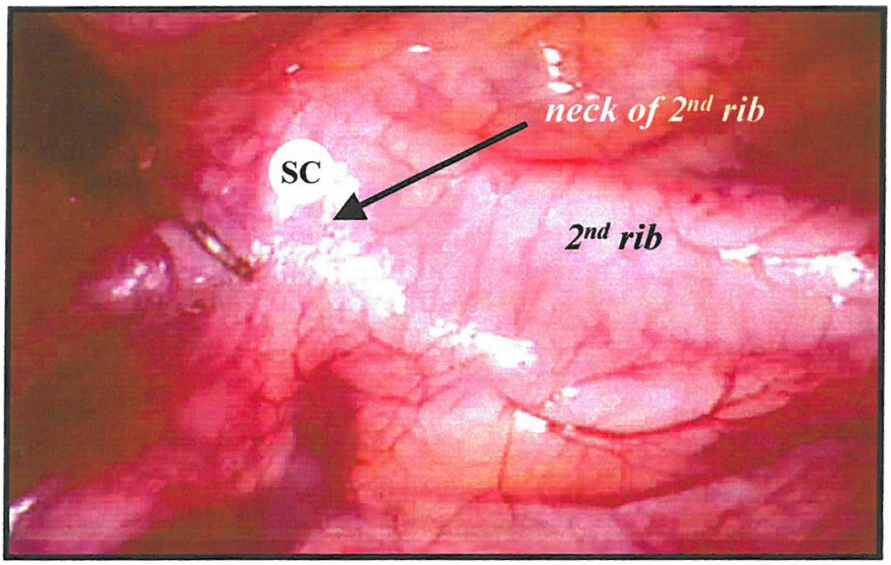


Plate 3 : *Left thoracoscopic sympathectomy* **:** *If the sympathetic chain (SC) is not readily seen it is easily palpable as a cord-like structure coursing over the neck of the 2nd rib*

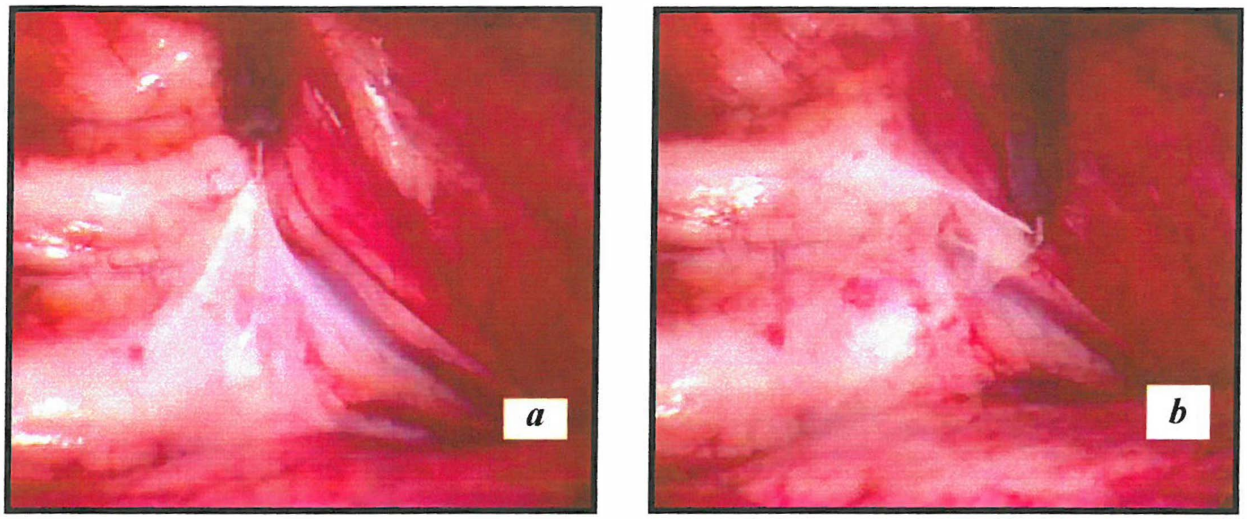


Plate 4 (a,b) : *The pleura overlying the right sympathetic chain is mobilized (after creating a pleural window using cautery)*

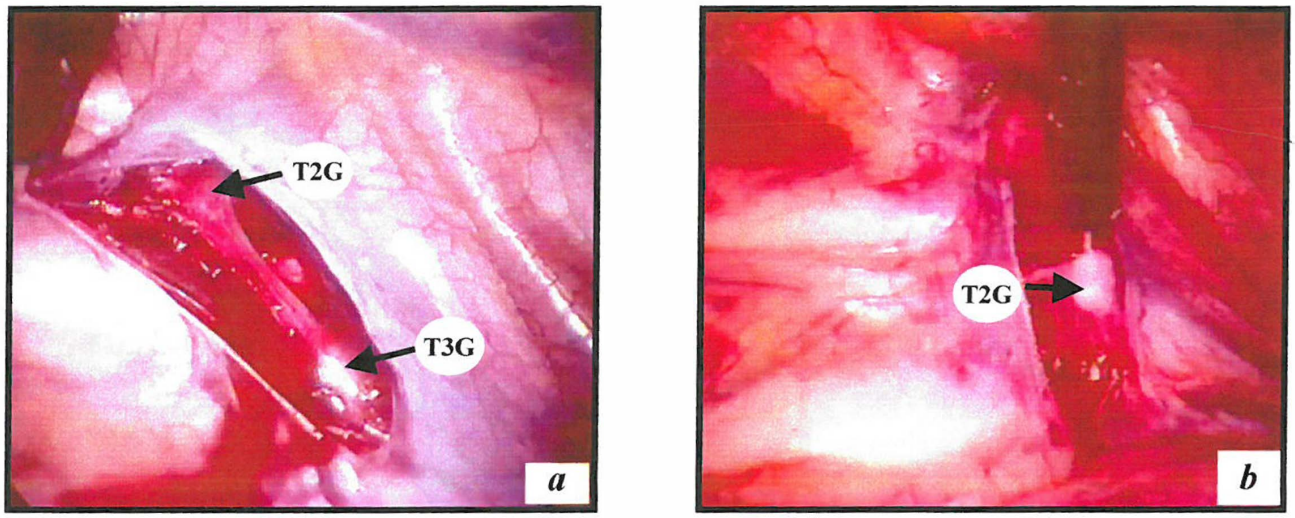


Plate 5 (a,b) : *The pleura overlying the right sympathetic chain is mobilized (after creating a pleural window using cautery)*

T2G	-	Second thoracic ganglion
T3G	-	Third thoracic ganglion

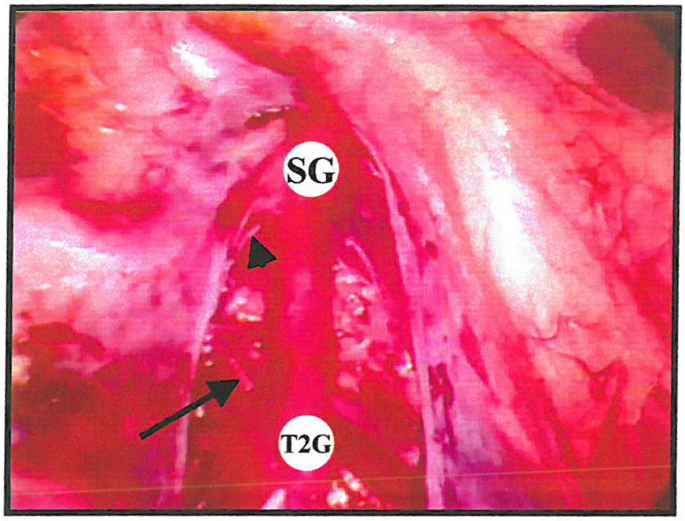


Plate 6 : *Right thoracoscopic sympathectomy : the pleural stripping has extended proximally to demonstrate the inferior component of the stellate ganglion (SG). Rami to the second thoracic ganglion (T2G) [⟶] and to SG [▶] are demonstrated*

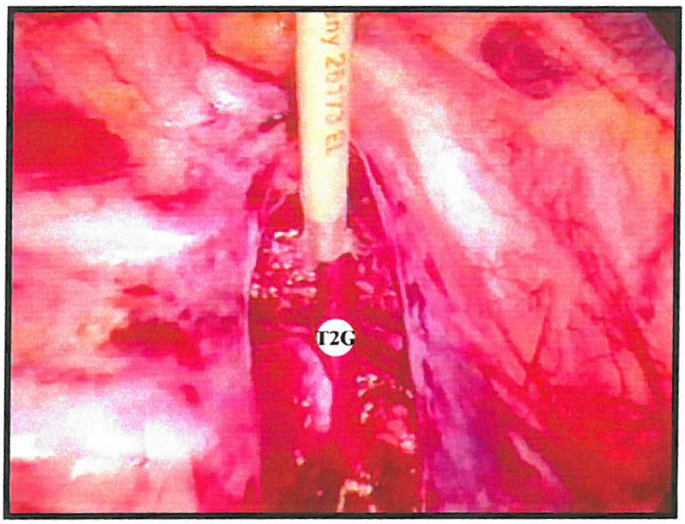


Plate 7 : *Right thoracoscopic sympathectomy : the sympathetic chain is transected proximally initially*

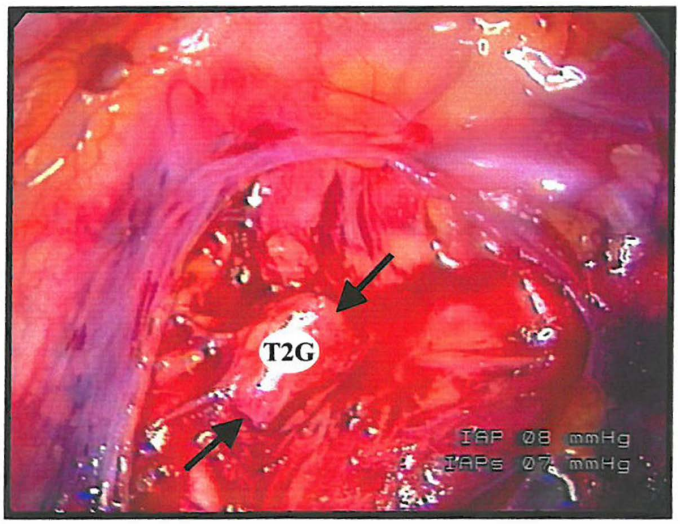


Plate 8 : *Left thoracoscopic sympathectomy : second thoracic ganglion (T2G) has been transected proximally and distally*

Troublesome bleeding from the posterior intercostal veins was controlled by the judicious use of cautery. These veins are variable in their arrangement, coursing both anterior and posterior to the sympathetic chain. They pose more of a problem in dissecting the right chain; here the 1st posterior intercostal vein tends to enter the operative field as it courses towards the superior vena cava. In contrast, on the left side, the 1st posterior intercostal vein is invariably lateral to the field of dissection, draining into the left subclavian or left brachiocephalic veins. The lower intercostal vein (2nd, 3rd or 4th) only become significant when more extensive ganglionectomies (3rd and 4th) are undertaken.. The technical exercise is aided by their pre-emptive cautery. The sympathetic chain, now mobilized from the 2nd to the 3rd rib, is transected above and below the 2nd thoracic ganglion. During the early period of the study, a more extensive ganglionectomy – up to the 3rd thoracic ganglion – was routinely undertaken. Currently, a limited (2nd thoracic) ganglionectomy is routine practice. The excised 2nd thoracic ganglion is retrieved for histological evaluation.

With homeostasis accomplished, the area of dissection was infiltrated with a local anaesthetic agent (Macaine®). The surgeon ensured that the CO_2 insufflation is stopped off : gentle suction is applied through the dissecting port.. A saline washout of the dissection site is only undertaken if pooled blood or a clot is noted. In concert with the suction gentle positive end expiratory pressure is applied by the anesthetist. The cannula with the telescope is steadily retracted in the face of the re-expanding lung. Prior to removing the cannula the lung should be seen to be herniating through the intercostal musculature as the camera cannula is withdrawn (Plate 9).

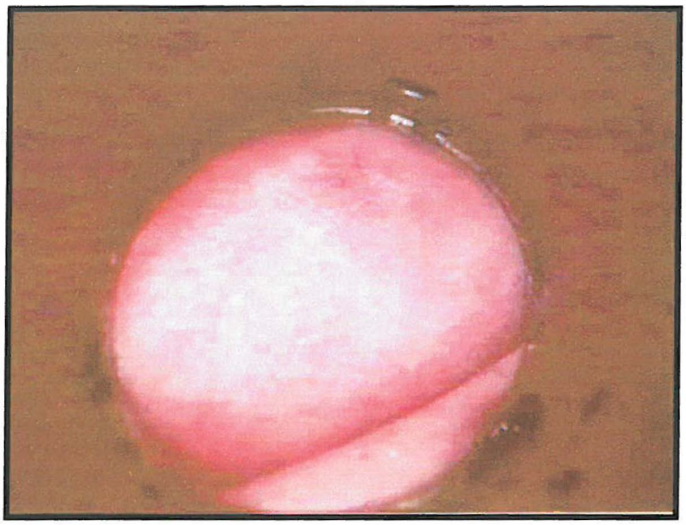


Plate 9 : *Herniation of expanded lung through port site facilitated by application of positive end expiratory pressure and aspiration of pneumothorax*

Closure of the port site is with absorbable sub-cuticular suture. Post-operatively patients are nursed in the general recovery bay. Blood pressure, pulse and oxygen saturation levels were routinely monitored. Analgesia was provided by Panado® and continuation of the non-steroidal anti-inflammatory suppository. Omnopon® was only administered if pain could not be controlled by these measures.

Intercostal chest drains were not routinely placed. Furthermore, post-operative chest radiographs were not routinely undertaken, being reserved for those instances of respiratory distress, progressive desaturation (SP O_2 < 95%) or unremitting or progressive surgical emphysema.

Following full recovery from the anesthesia, the patients are transferred to the general ward; by the evening of the procedure (usually 8-9 hours following the procedure), the patients were discharged home. Patients were only kept overnight if there was clinical concern (eg. developing pneumothorax or haemothorax) or patient lived in an area remote from the medical facility.

If the patient required bilateral sympathectomy, the procedure was repeated on the contralateral side under the same anesthetic. The post-operative care was not different from those undergoing a unilateral procedure.

OPEN SYMPATHECTOMY

The preferred approach for open sympathectomy is the Telford supraclavicular approach (Telford, 1935) (Figure 8). In patients with CRPS, skin positioning, preparation and draping should be arranged in anticipation of a conversion to the open approach. The necessary instrumentation must be readily available. The sympathetic chain is dissected and transected as in the thoracoscopic procedure. Diathermy is used with caution. The excised 2nd thoracic ganglion is sent for histology.

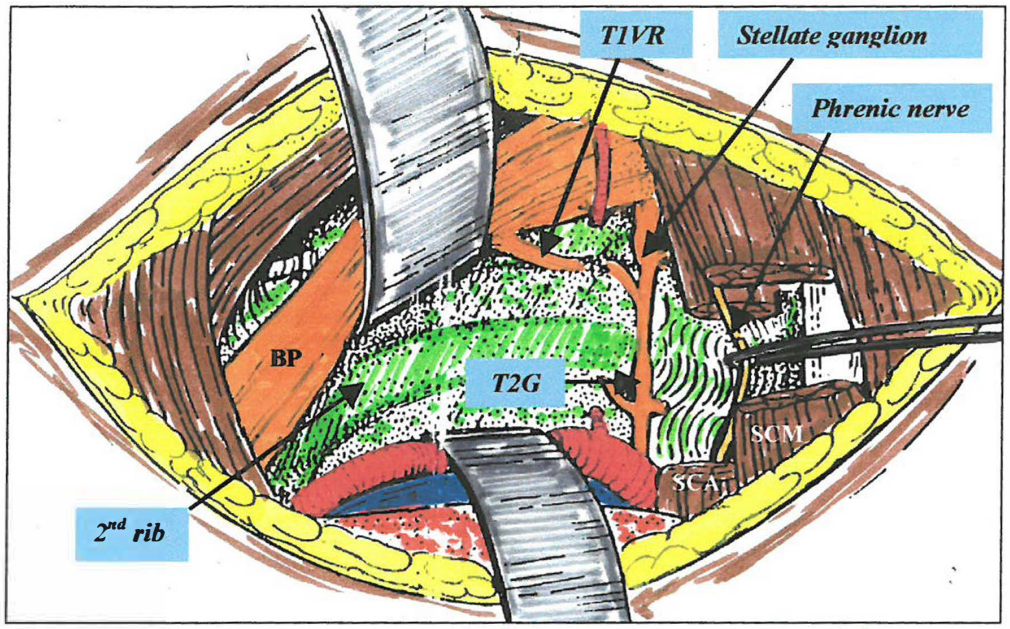


Figure 8 *: Supraclavicular approach to the 2nd thoracic ganglion after Rintoul (1995)*

SA	-	Subclavian artery	**BP**	-	Brachial plexus
SV	-	Subclavian vein	**T1VR**	-	T1 ventral ramus
SCM	-	Sternocleidomastoid muscle	**SCA**	-	Scalenus anterior muscle
T2G	-	2nd thoracic ganglion			

Recourse to the open approach should always be anticipated in those patients in whom lung collapse – crucial to an adequate thoracopscopy – cannot be procured. This includes patients with a history of chronic lung disease eg. pulmonary tuberculosis, history of lung trauma or previous thoracotomy. This prepares the scrub nurse for the prospect of an operation (therefore positioning and preparing the appropriate site for open surgery and having the relevant instruments available). The surgeon is also prepared for the potentially more challenging open procedure.

3.2.1 OPEN VERSUS THORACOSCOPIC SYMPATHECTOMY

Patients undergoing endoscopic transthoracic cervical sympathectomy for primary hyperhidrosis were prospectively recruited for evaluation (Group I). These were compared to a retrospectively collected age-matched group of the most recently undertaken open cervical sympathectomy for palmar hyperhidrosis (Group II). This investigation was conducted at the RK Khan and King Edward VIII Hospitals, Durban. The procedures were undertaken by experienced surgeons competent in both the thoracoscopic and the open approach. The inclusion and exclusion criteria have been described.

Factors evaluated were :

i. operating time in minutes

ii. hospital stay in days

iii. opioid usage

iv. return to normal activity

v. cost analysis comparing open *vs* thoracoscopic sympathectomy

Group I patients underwent thoracoscopic sympathectomy under general anaesthetic with single lumen endotracheal intubation. The thoracoscopic technique was standard and has been described.

Group II patients underwent the standard Telford procedure undertaken via the supraclavicular approach.

Statistical analyses was performed using the Student T Test and the Fischer Exact Test.

In both groups of patients the procedures were undertaken bilaterally during the same anaesthetic. Both procedures entailed excision of the 2nd thoracic ganglion that was sent for histopathological assessment.

3.2.2 ANESTHETIC CONSIDERATIONS : SINGLE LUMEN ENDO-TRACHEAL INTUBATION VERSUS DOUBLE LUMEN ENDOBRONCHIAL INTUBATION FOR THORACOSCOPIC SYMPATHECTOMY

With ethical approval and informed consent, 20 patients between the ages of 15 – 30 years undergoing thoracoscopic sympathectomy for palmar hyperhidrosis were prospectively randomized after a standard general anesthetic to have either a single lumen or double lumen intubation. This investigation was undertaken at the King Edward VIII Hospital.

The anesthetic in both groups was administered by a senior anesthetist. Diprivan® (2mg/kg) was used for induction of anaesthesia; intra-operative analgesia was provided by Sufenta® (0.5mg/kg) and infiltration of the port sites with Macaine®. A non-depolarizing short acting muscle relaxant, (Nocuran® 0.1mg/kg) was used.

Routine monitoring used included electro-cardiography, non-invasive blood pressure, oxygen saturation, end-tidal CO_2 concentration, ventilator disconnect and low inspired O_2 concentration alarm.

In both groups the patients were placed in a 30° reverse Trendelenberg position with the arms widely abducted.

Patients in Group I had a double lumen endobronchial tube passed to allow selective deflation of the ipsilateral lung. This involved clamping the bronchial catheter mount and

opening the tube lumen to atmosphere. A Veress needle was then introduced through the axilla via a small incision in the 3rd intercostal space. Carbon dioxide insufflation was effected to attain an intra-pleural pressure of 7cm H_2O. Contralateral lung ventilation was maintained mechanically to maintain oxygen saturation to at least above 97-98% .

Patients in Group II were intubated with a single lumen endotracheal tube. The patients were slightly hyperventilated by keeping the end-tidal carbon dioxide concentration at 30-35mm/kg. The patients were then kept apnoeic and the lung partially collapsed by disconnecting the anesthetic circuit before the Veress needle was introduced into the 3rd intercostal space. This step was necessary to avoid iatrogenic injury to the lung. Carbon dioxide insufflation to the inpsilateral pleural space was continued to a preset value of 7cm H_2O.

The patients were maintained on shallow, manual ventilation. Visualization of the proximal sympathetic chain was further expedited by the surgeon depressing the apex of the lung caudally with the telescope. Anesthesia was maintained with 100% oxygen and a hypnotic agent (Isoflurane®).

In both groups, at the completion of the ganglionectomy, the area of dissection was infiltrated with Macaine®. Lung re-expansion was facilitated by the application of positive end expiratory pressure by the anesthetist and by the concomitant aspiration of the pleural space (by gentle suction) undertaken by the surgeon. Intercostal chest drains were not routinely placed.

In addition to the demographic data, the following were evaluated :

- episodes of desaturation ($Sp0_2$<95%)
- hypotension (systolic BP < 90 mmHg)
- post-operative pain score evaluated on a Visual Linear Analogue Scale
- the need for supplementary analgesia
- incidence of complications were noted.

Post-operatively patients were administered Panado® and a non-steriodal anti-inflammatory agent. Opiate analgesics were administered when pain was persistent.

Statistics were performed using the Fisher's Exact Test.

3.2.3 LIMITED GANGLIONECTOMY : A PROSPECTIVE EVALUATION

This evaluation was conducted at the King Edward VIII Hospital, Durban. All patients presenting with socially or functionally incapacitating Primary Hyperhidrosis during a 14-month period (February 1997 – March 1998) were prospectively evaluated. At the initial assessment the patients demographics (age and sex) and distribution of the hyperhidrosis were noted. The severity of the hyperhidrosis as well as the outcome was scored on a linear analogue scale (LAS) from 0 to 10. The score of zero represented complete anhidrosis or complete satisfaction; the score of 10 represented dripping hyperhidrosis or total dissatisfaction with the outcome.

The spectrum of the presenting hyperhidrosis was further categorized as being mild (1-3), moderate (4-6) or severe (7-10). Likewise, the outcome following surgery was quantified as excellent (1-3), satisfactory (4-6) or poor (1-3).

The pre-operative evaluation of these patients has been outlined. The operative technique, which was consistently used, has also been detailed.

All patients were reviewed at one week and then at 3 monthly intervals until the end of the study period. At this time an independent assessor evaluated patients for outcome and side-effects, specifically compensatory hyperhidrosis. The extent of the compensatory hyperhidrosis was assessed using a LAS (see above).

Statistical analysis was performed by the paired Students t test.

3.2.4 OUTCOME TO THORACOSCOPIC SYMPATHECTOMY : MECHANISMS FOR FAILURE

All patients who were subjected to thoracoscopic sympathectomy for debilitating primary hyperhidrosis between 1992-2001 were evaluated for early and late sympathetic failure. Patients who had sympathectomy undertaken for other indications (eg. chronic regional pain syndrome and Raynaud's phenomenon) were not enrolled, owing to the unpredictable outcome to sympathectomy in these conditions.

The thoracoscopic approach was the preferred method to effect upper limb sympathetic denervation. There was a standard technique for thoracoscopic sympathectomy ; this technique has been detailed. The excised 2nd ganglion was routinely sent for histology.

Outcome to thoracoscopic sympathectomy was quantified on a linear analogue scale (LAS) from zero to ten. The score of zero represented complete anhidrosis or complete satisfaction; the score of ten represented dripping hyperhidrosis or total dissatisfaction with the outcome.

Patients were evaluated at 1 week and then at 3 monthly intervals for a year. Patients were advised to return if they suspected or developed recurrence of the hyperhidrotic state.

3.3 ANATOMICAL CONSIDERATIONS

3.3.1 ALTERNATE NEURAL PATHWAYS

An anatomical evaluation of the cervico-dorsal sympathetic chain (its variations and connections) appropriate to upper limb sympathetic supply using standard dissection techniques was undertaken.

Location of Study

The adult human specimens used in this study, were obtained using cadaveric material (in accordance with the Human Tissue Amendment Act, 51 of 1989) from the Department of Anatomy, School of Basic and Applied Medical Sciences, University of Durban-Westville and Department of Anatomy, Nelson R Mandela School of Medicine, University of Natal, and the Department of Human Biology, Technikon Natal. Ethical permission to undertake this study was obtained from the Research and Ethics Committee, University of Natal.

Participants

Dissections were conducted in adult human cadavers. Cadavers displaying cervical trauma, evidence of previous surgical exploration or macroscopic pathology were excluded.

Technique

A midline incision was made from the lower border of the mandible to the sternal angle. The skin, together with the platysma muscle was reflected and all superficial muscles (sternocleidomastoid, pectoralis major, pectoralis minor, omohyoid, sternohyoid and

sternothyoid muscles) were excised. The rib cage was removed after incision of the ribs along their mid axillary line. The clavicle was removed after both the acromio-clavicular and sternoclavcular joints were cut. The brachial plexus was dissected as far medially as their roots and laterally to the cords after removal of scalenus anterior muscle.

The thoracic and abdominal cavities were eviscerated to expose their posterior walls. Parietal pleura was gently stripped bilaterally to reveal the sympathetic chain. All neural connections between the sympathetic chain (from ganglia and interganglionic segments) and intercostal nerves were micro-dissected from the stellate ganglion superiorly to the 3rd thoracic ganglion distally to display the location and configuration of these and intermediate ganglia. Dissections were undertaken to display all neural connections from the sympathetic chain (including ganglionic and interganglionic segments) to adjacent ventral rami. Neural connections i.e alternate neural pathways between the adjacent rami were be identified; their precise course and distance from the sympathetic chain (in millimeters) were recorded on a schematic representation of the sympathetic chain.

The precise location of the stellate ganglion and its incidence were documented. The incidence of ganglionic fusion i.e stellate to 2nd thoracic, 1st to 2nd thoracic, 2nd to 3rd thoracic ganglionic fusion were recorded.

3.3.2 STELLATE GANGLION BLOCK : AN ANATOMICAL RE-APPRAISAL

The study was conducted at the Department of Anatomy, University of Durban-Westville. Permission to undertake the study was obtained from the University's Ethics Committee. The sympathetic block technique was a modification of the blind paratracheal approach.

Technique : The procedure was performed by an anesthetist accomplished in performing sympathetic blockade of the upper limb and the anesthetist standing behind the cadaver. With the neck fully extended, the surface landmark for the transverse process of the 6^{th} cervical vertebra was defined. The accuracy of this location was confirmed by the palpation of the Chassaignac Tubercle, the bony landmark for the 6^{th} cervical transverse process. The sternocleidomastoid muscle and the carotid sheath are retracted downwards and laterally. A 23 gauge needle is inserted perpendicularly into the skin at the described landmark; the needle is then advanced infero-medially until the tip impinges upon the antero-lateral aspect of the body of the 7^{th} cervical vertebra. The needle is then withdrawn approximately 5mm such that its tip now overlies the underlying longus colli muscle. Ten 10mls of Toludine Blue Solution was then slowly injected (over 2 minutes) (Figure 9).

Cadavers who had surgery, trauma or gross pathology in the supra-clavicular region were excluded from the study.

Thirty minutes following the delivery of the injectate a median sternotomy was perfomed. The lungs were gently displaced antero-medially; great care was undertaken to ensure that the pleura, particularly the apical and mediastinal pleura, was not disturbed. The extent of

the spread of the Toludine Blue Solution- medial, lateral, superior and distal- and the relation of the spread to the sympathetic ganglia and chain was noted.

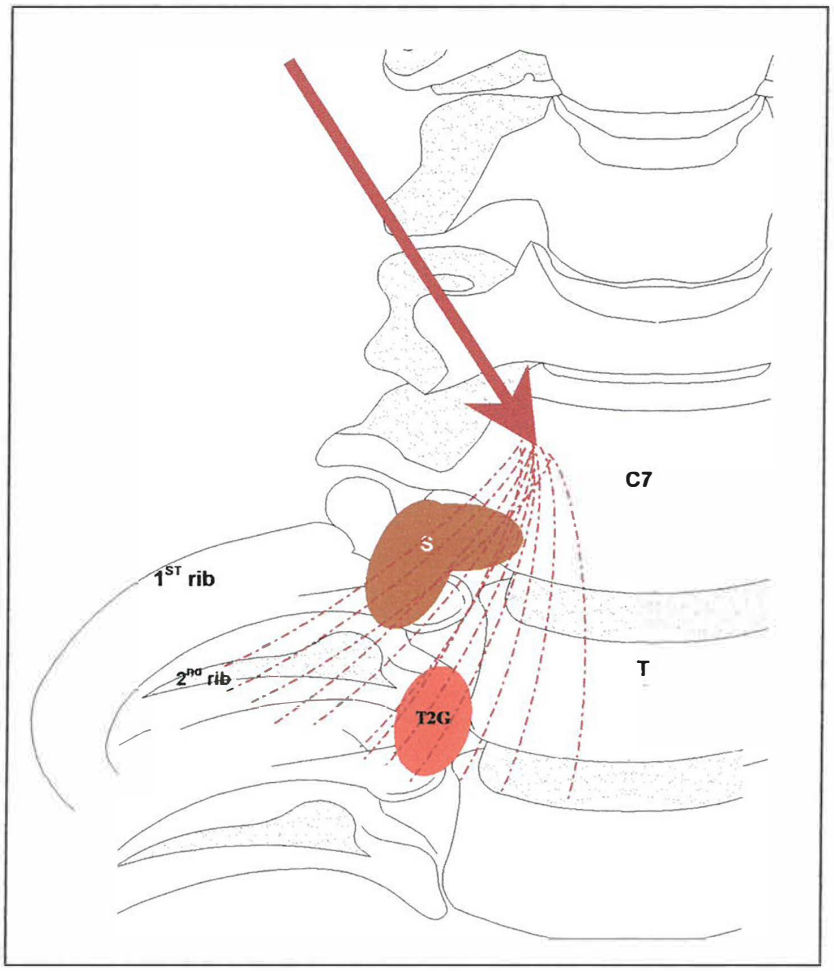


Figure 9 *: Direction of injection and injectate spread at stellate ganglion block*

SG	-	Stellate ganglion
T2G	-	2nd thoracic ganglion
C7,T1	-	7th cervical; 1st thoracic vertebrae

3.4 PATHOLOGICAL CONSIDERATIONS

Patients successfully undergoing surgery for primary hyperhidrosis and CRPS Type II at King Edward VIII Hospital, Durban during the period spanning January 1999 to December 2000 were enrolled into this study. All patients had an excision of the 2nd thoracic ganglion either at thoracoscopy or at open surgery. At surgery, there was minimal manipulation, traction or cautery applied to the sympathetic chain. Following its excision, the ganglion specimen was placed in formalin solution.

The ganglion specimens were harvested from

- Ten consecutive patients who had the 2nd thoracic ganglia excised for primary hyperhidrosis
- Ten consecutive patients who had a 2nd thoracic ganglion excised for CRPS and,
- Five specimens were retrieved from fresh cadavers from the forensic mortuary at Pinetown, Durban.

All specimens taken from patients were with informed consent. Cadaver specimens were taken after securing ethical approval in accordance with the Human Tissues Act 51 of 1989 of South Africa.

All ganglia were subjected to histological examination to confirm that the tissue was of ganglionic origin. The standard and immunopathological examinations of the ganglia were undertaken at the Department of Anatomical Pathology, University of Natal.

Biopsied tissue was fixed in 10% formol saline and underwent processing in an automated tissue processor for approximately 15 hours. Biopsied tissue samples that have been embedded in molten paraffin wax and cast into a block a solidified wax were used for the further section and slides.

The cell surface markers evaluated (using the immunoperoxide microwave staining technique) were:

- CD 3 - thymocyte cell receptor
- CD 4 - T helper cell marker
- CD 8 - T cytotoxic cell marker
- CD 20 - mature B cell marker
- CD 68 - macrophage marker
- LCA - CD 45 - Leucocyte Common Antigen

Technique for evaluating the cell surface markers

Block specimens were then cut into 2μm sections and mounted on poly-L-lysine coated slides (Sigma Diagnostics Inc.). The slides were then heat fixed at 60° C for approximately 15 minutes. The sections were then deparaffinized and rehydrated with water.

Slides were then placed in antigen retrieval solution (0.01 M trisodium citrate buffer, pH 6.00) for 10 minutes at 85° C in a microwave.

The sections were cooled to room temperature and this usually took between 5 to 10 minutes. The slides were then washed well under water.

Thereafter, the slides were placed in 3% H_2O_2 for 5 minutes at room temperature. The slides were then washed well under water and then placed in a Phosphate Buffered Saline (PBS) bath.

CD3 mAb (Dako, code A0452) was used in a dilution of 1:50 and CD20 (Dako, Clone L26, code M0755) was used in a dilution of 1:70. Dilutions were done with Bovine Serum Albumin. Slides were incubated in primary antibody for 4 minutes and 30 seconds at low temperature in a microwave oven. This is equivalent to 37°C. Thereafter slides were allowed to stand at room temperature for 10 minutes.

Slides were washed well in 3 changes of PBS and thereafter placed in a PBS Bath. The slides were then incubated in Biotinylated Link (Dako LSAB2 system) for 3 minutes and 30 seconds on low temperature in the microwave oven. Slides were again washed thrice in PBS and placed in a PBS bath.

The slides were then incubated in substrate-chromogen solution (DAB, Dako Chromogen substrate buffer) for between 3 to 5 minutes. Thereafter the slides were washed well with tap water. The nuclei were then stained in Mayer's Haemotoxylin for 1 minute and 30 seconds. Slides were again washed well in water. Blue nuclei in ammoniated water. Slides were again washed well in water. Slides were then dehydrated, cleared and mounted.

A similar protocol was performed for the CD68 mAb (Dako, clone Kpi, code M0814) but the dilution was 1:200 using BSA and the stand time after incubation in the microwave oven was 1 minute. LCA (CD45) [Dako, clone 2B11 + PD7/26, code M0701) was used in a dilution of 1:60 effected using PBS and the stand time was the same as for CD68. Slides were prepared as above for CD4 (Novocastia Laboratories, Newcastle upon Tyne, UK; clone IF6, code NCL-CD4-IF6), and CD8 (Novocastia Laboratories, Newcastle upon Tyne, UK; clone 4B11, code NCL-CD8-4B11) except following deparrafinization, the slides were incubated in 0.5% H_2O_2/methanol for 10 minutes at room temperature. The slides were then placed in Antigen Retrieval Solution (1mM EDTA) for 10 minutes at 85°C in the microwave oven. The slides were then cooled to room temperature for about 5 minutes. The slides were then washed well in tap water and placed in a PBS bath. Slides were then incubated in normal serum for 20 minutes at room temperature. The slides were then placed in the primary antibody (dilution 1:30) for 4 minutes and 30 seconds at low temperature in the microwave oven. The slides were then allowed to stand for 50 minutes at room temperature. Slides were thereafter washed in PBS and then incubated with biotinylated link for 3 minutes and 30 seconds at low temperature in the microwave oven. Thereafter, the slides were allowed to stand at room temperature for 5 minutes. Slides were thereafter washed well in PBS. The slides were then incubated for 3 minutes 30 seconds at low temperature in the microwave oven in Streptavidin-HRP. The slides were then allowed to stand at room temperature for 5 minutes. The slides were again washed well in PBS and then incubated in Substrate-Chromogen Solution (DAB-Dako Chromogen/ Substrate Buffer) for between 3 to 5 minutes at room temperature. The slides were then washed well under tap water. The nuclei were stained in Mayer's Haematoxylin for 90 seconds. The slides

were again washed well under tap water. Blue nuclei in ammoniated water. The slides were again washed well under tap water. These cells were dehydrated, cleared and mounted.

Cell surface marker counts

Cell surface markers were counted in a higher power field (HPF) over 10 areas on the slide and the average result was taken. This was then done on 5 occasions for each slide and the average of this was taken as the final result. An experienced histopathologist, blinded to the clinical background of the submitted ganglia, evaluated all slides on all 5 occasions.

Ethical approval was obtained from the Ethics Committee of the Nelson R Mandela Medical School, University of Natal.

Statistical analysis was carried out using SPSS 9.0 for windows (BMDP statistical software, Los Angeles, CA). Data was entered directly onto SPSS. Results were expressed as medians and range. The statistical significance of the differences between the median values was evaluated using the Mann Whitney U test. A p value of <0.05 was considered to be significant.

CHAPTER 4

RESULTS

4.1 SAMPLE DEMOGRAPHICS

Between May 1992 to September 2001, a total of 498 patients presented for upper limb sympathectomy. A total of 939 operations were undertaken. Palmar hyperhidrosis was by far the commonest indication for upper limb sympathectomy. The indications for sympathectomy, the numbers of patients presenting and operations undertaken for various conditions are indicated in Table 6 and Figure 10.

TABLE 6 : *FREQUENCY (%) OF SYMPATHECTOMIES UNDERTAKEN : 1992-2001*

	Number of Patients (%)	Number of Operations (%)
Palmar Hyperhidrosis	448 (89.9)	884 (94.1)
Chronic Regional Pain Syndrome	42 (8.5)	43 (4.6)
Raynaud's Disease	5 (1.0)	9 (1.0)
Peripheral Vascular Disease	3 (0.6)	3 (0.3)
TOTAL	**498**	**939**

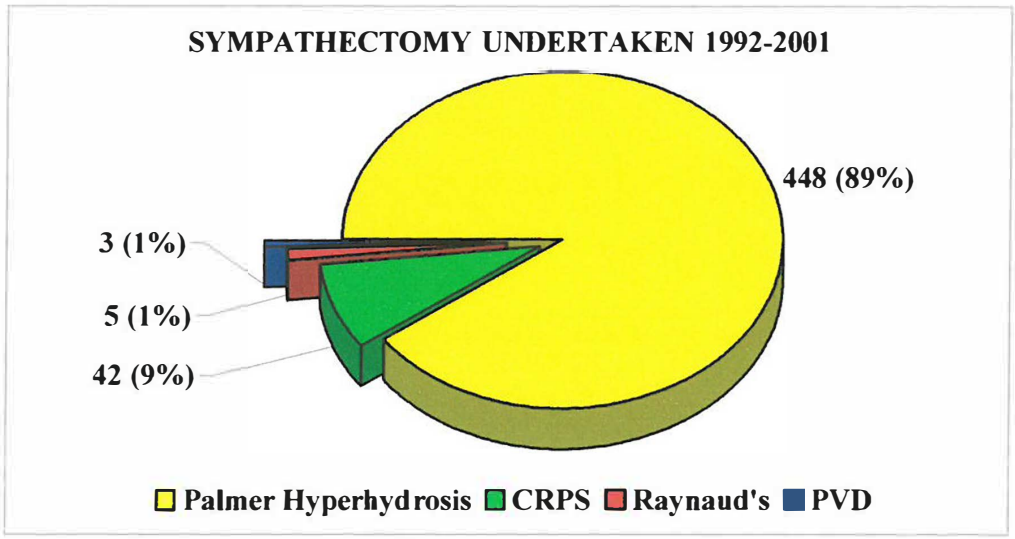


Figure 10 : *Patients presenting for sympathectomy - indications*

4.1.1 PALMAR HYPERHIDROSIS

Between May 1992 to September 2001, a total of 448 patients presenting with palmar hyperhidrosis (Plate 10) were considered suitable for thoracoscopic sympathectomy. Table 7 summarizes the experience between 1992 and 2001 (Appendix 1).

TABLE 7 : *FREQUENCY OF THORACOSCOPIC SYMPATHECTOMIES FOR PALMAR HYPERHIDROSIS*

YEAR	PATIENTS	OPERATION
1992	17	34
1993	39	78
1994	42	83
1995	61	121
1996	56	109
1997	59	116
1998	68	134
1999	57	113
2000	31	61
2001	18	35
TOTAL	**448**	**884**

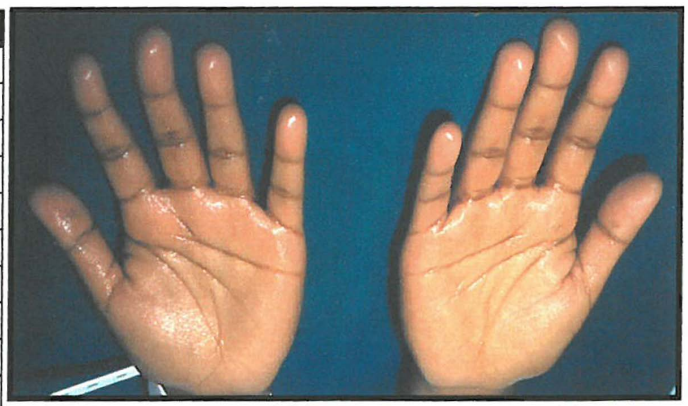


Plate 10 : *Palmar hyperhidrosis – typical presentation*

Associated axillary hyperhidrosis was noted in 226 patients (50.4%); associated plantar hyperhidrosis was encountered in 358 (79.9%). When present, axillary and plantar hyperhidrosis were always subordinate to palmar hyperhidrosis as the presenting problem. In all but 2 patients, the palmar hyperhidrosis was bilateral. In these 2 patients presenting with unilateral hyperhidrosis, both patients had undergone thoracoscopic sympathectomy previously. One patient had recurrent palmar hyperhidrosis following a period of anhidrosis; the other patient had persistent palmar hyperhidrosis following an apparent successful thoracoscopic sympathectomy. One patient presented with persistent bilateral palmar hyperhidrosis also following an apparently successful procedure.

There were 249 males and 199 females. The mean age at presentation was 19.2 years (range 13-52 years). The means Visual Linear Analogue Scale Score for palmar hyperhidrosis on presentation was 9.1 (range : 8.7-10).

Thoracoscopic sympathectomy was successfully undertaken in 448 patients (884 procedures). In 6 patients, thoracoscopic sympathectomy was performed successfully, unilaterally; of these, 2 patients had either recurrent palmar hyperhidrosis (n=2) or persistent hyperhidrosis (n=4). In the other 6 patients successfully undergoing unilateral thoracoscopic sympathectomy, dense pleural adhesions precluded the attainment of an adequate lung collapse to facilitate safe thoracoscopy. This prompted the abandonment of the procedure. Thus, a total of 884 (out of a possible n=890) procedures were successfully undertaken.

In all patients in whom thoracoscopic sympathectomy was successfully accomplished (n=884) the clinical outcome was excellent. In the vast majority of patients (n=882), complete palmar anhidrosis was reported immediately following the procedure and at the one week review; three patients reported unilateral persistence of palmar hyperhidrosis that disappeared within a fortnight of the procedure. The overall success rate was 99.7%. Review at three months by personal and telephonic interview was possible in 395 patients (89%). The successful effect of sympathectomy at the one week review was noted to have persisted. However, in 2 patients, recurrent sympathetic activity (rSA) developed after 6 months; the details of these patients and their outcome to further management are detailed in Chapter 4.2.4.

Compensatory Hyperhidrosis

Compensatory hyperhidrosis developed in 56 patients (12.6%); this was usually evident at the three month review. This sweating was unpredictable and manifested in circumstances similar to those predisposing to palmar hyperhidrosis. Invariably the front and back of the chest, trunk and thighs were affected. All 56 patients were severely distressed by this side effect, notwithstanding the pre-operative cautioning about this. Twenty-two patients (4.9%) were so distressed by this compensatory hyperhidrosis that they regretted the procedure, even though the palms were now dry. In the remaining 34 patients the compensatory hyperhidrosis was moderate; these patients accepted this side-effect and given the successful outcome of the palmar hyperhidrosis, were satisfied with the outcome.

Gustatory Sweating

Gustatory sweating developed in 2 patients; this effect was noted to develop 3 months following sympathectomy. Whilst the symptoms regressed spontaneously in one patient over the ensuing 9 months, in the 2nd patient with this affliction the symptoms persisted.

Anaesthetic effects during thoracoscopic sympathectomy

A sudden bradycardia (28 beats per minute and 18 beats per minute, respectively) developed in 2 patients. Both patients were fit, young (<24 years old) and with no history of cardiac disease. No anaesthetic reason could be found for this. In both patients, the procedure was undertaken initially on the left side, contrary to the policy of always undertaking right sympathectomy initially. Further manipulation of the sympathetic chain was stopped. In both patients, no pharmacological agents apart from Atropine were administered to regain sinus rhythm which returned within 2 and 3

minutes, respectively. The procedure was thereafter continued uneventfully. On transection of the sympathetic chain, no changes were noted with respect to pulse, blood pressure, respiratory rate or oxygen saturation. The post-operative recovery in both patients was uneventful.

Complications (Table 8)

i. Haemothorax : One patient developed a haemothorax; this was confirmed on day one post-surgery with the patient complaining of right sided discomfort and dyspnoea. Intercostal chest drainage had to be instituted over the ensuing two days.

ii. Pneumothorax : Pneumothorax presenting with persistent dyspnoea immediately following surgery was noted in one patient. With the insertion of an intercostal chest drain, this improved within 24 hours. Surgical emphysema developed in 7 patients. This was always confined to the lateral chest wall, adjacent to and between the port sites. In 4 patients, an underlying apical pneumothorax less than 2cm from the thoracic apex was noted on chest radiography. Since there was no associated respiratory embarrassment, these patients were managed conservatively.

iii. Horner's Syndrome : A Horner's Syndrome developed unilaterally (right side) in one patient. This patient developed meiosis, ptosis and rhinitis. The surgical procedure was reported to be uncomplicated; the 2^{nd} thoracic ganglion was readily recognized. Neither excessive traction nor diathermy was applied to the sympathetic chain. The Horner's Syndrome was noted on day one post-surgery. Over the ensuing months, the signs gradually improved so that corrective surgery was not necessary.

iv. Hospital Stay : The majority of patients (435 patients; 97.9%) were discharged within 24 hours of admission. Nine patients had a longer hospital stay, either requiring intercostal chest drainage (2 patients) or the observation of surgical emphysema (7 patients). The two patients requiring intercostal chest drainage each stayed in hospital for two and three days, respectively; those patients with surgical emphysema stayed in hospital for at least two days after chest radiography had excluded the progression of a pneumothorax.

v. Return to work : All patients who were discharged within 24 hours of the procedure were able to return to work or study within 5 days of admission. Two hundred and forty nine patients (56.2%) were able to return to activity within 3 days. Those patients requiring intercostal drainage or observation of surgical emphysema returned to activity at a mean period of 12 days (range : 7-16 days).

TABLE 8 : *COMPLICATIONS FOLLOWING THORACOSCOPIC SYMPATHECTOMY FOR PALMAR HYPERHIDROSIS*

COMPLICATION	PATIENTS (n=448)	% OF PROCEDURES (n=884)
Haemothorax	1	0.1
Pneumothorax		
Requiring drain	1	0.1
No drain	4	0.5
Horner's Syndrome	1	0.1
Surgical emphysema	7	0.8
Atelectasis	0	0
Compensatory hyperhidrosis	56	12.6
Gustatory sweating	2	0.2
Persistent sympathetic activity	3	0.3
Recurrent sympathetic activity	3	0.3

4.1.2 CHRONIC REGIONAL PAIN SYNDROME

A total of 42 patients underwent upper limb sympathectomy. The median duration of symptoms was 9.5 (range 4 – 200) weeks at the time of presentation for surgery. There were 27 males; the median age was 32 (range 17 – 64) years. The median duration of symptoms in patients in Group1 (n = 24; symptoms < 3 months) was 6.5 (range 4 – 11) weeks. The median duration of symptoms in patients in Group 2 (n = 18; symptoms > 3 months) was 26.5 (range14 – 200) weeks (Plate 11) (Appendix 2 (i), 2 (ii)).

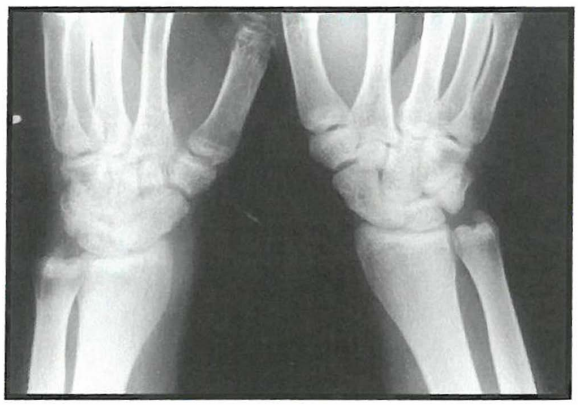


Plate 11 : *Late CRPS (> 12 months) – radiological effects. Note the marked osteoporosis affecting the left hand*

TABLE 9 : *RESULTS OF SYMPATHECTOMY FOR CHORNIC REGIONAL PAIN SYNDROME*

	Group I (%)[n = 24]	Group II (%)[n = 18]	*p value*
Excellent	17 (80.9)	3 (23.5)	
Good	7 (19.0)	5 (29.4)	
Satisfactory	0	3 (11.8)	
Satisfactory clinical outcome	24 (100)	11 (64.7)	<0.001
Poor clinical response	0	7 (35.3)	<0.003

Surgery (Table 9)

Sympathectomy was successfully performed in all patients referred for the procedure. Thoracoscopic sympathectomy was attempted in all patients. This was successful in 30 patients. In 12 patients, sympathectomy had to be performed by the open route. In the latter group, the thoracoscopic approach was abandoned either because of dense adhesions involving the lung apex or pleural thickening totally obliterating an adequate view of the proximal sympathetic chain.

The higher rate of open sympathectomy in Group 2 patients correlated with the larger number of SGB administered to this group compared to the patients in Group1. Patients in group1 had a median of 1 (range 1 – 2) blocks and patients in group2 had a median of 3.5 (range 1 – 5) blocks administered.

Predictive value of SGB

Of the 42 patients referred for surgery, only 25 patients had appreciable pain relief from SGB that confirmed the presence of sympathetic mediated pain. In the remaining 17 patients there was no response to SGB.

In the 25 patients who had relief from SGB, the outcome following sympathectomy was noted to be poor in 5 patients; In the 17 patients with a poor response to SGB, the outcome was noted to be excellent in 6 patients.

Pain response to sympathectomy

The overall improvement in all 42 patients from a median preoperative score of 9.0 (range 7 – 10) to a median postoperative score of 2.0 (range 0 – 9.4) was noted to be significant ($p<0.001$, Wilcoxon signed rank test) (Figure 11).

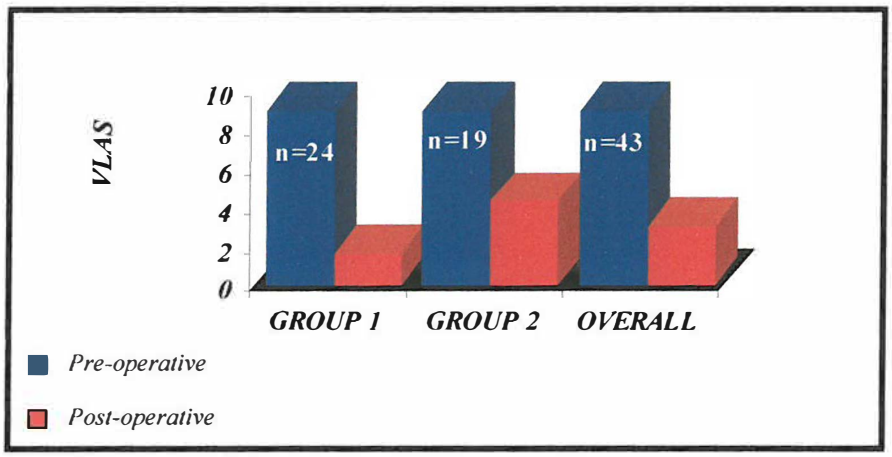


Figure 11 *: Mean outcome to sympathectomy in Group I, Group II and Overall*

The clinical improvement in VLAS in Group 1 patients was a decline from a median preoperative score of 9 (range 7.5 – 10) to a median postoperative score of 1.65 (range 0 – 4.2) (Figure 12). Due to the minimal impact of pharmacotherapy and progressive debility, SGB was undertaken in 2 patients within 4 weeks of commencement of therapy.

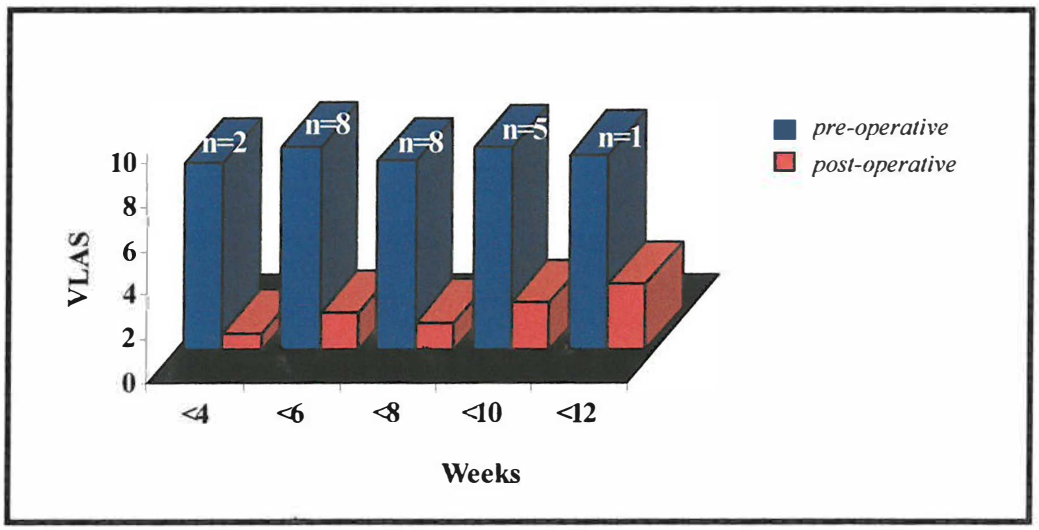


Figure 12 : *Outcome to Sympathectomy in Group I*

In patients in Group 2, the clinical improvement was a decline from a median preoperative score of 9.1 (range 7 – 10) to a median postoperative score of 4.2 (range 0.2 – 9.4) (Figure 13).

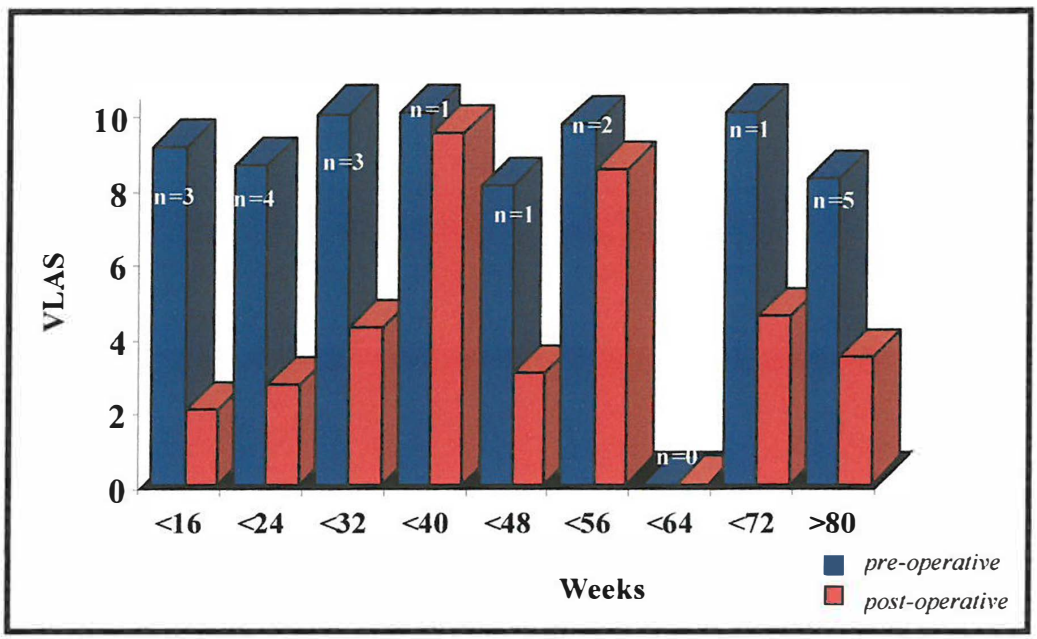


Figure 13 : *Outcome to Sympathectomy in Group II*

The outcome in Group 1 versus Group 2 was noted to be significantly better in the former group ($p<0.003$, Mann-Whitney U test).

The poorest results were in 7 patients from Group 2 who had been symptomatic for between 29 to 192 weeks.

The beneficial effect noted on day 10 following sympathectomy persisted during the median follow-up period of 40.6 (2 – 73) months. Three patients were lost to follow-up.

Surgical outcome

All patients who had thoracoscopic sympathectomy were discharged within 24 hours of admission. There were no complications following the procedure (Plates 12 a, b).

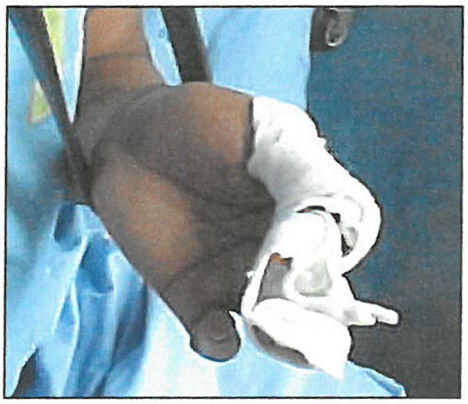


Plate 12 (a) : *Pre-operative presentation of CRPS (Group I patient, history of 8 weeks) - note the arm support and bandaging applied by*

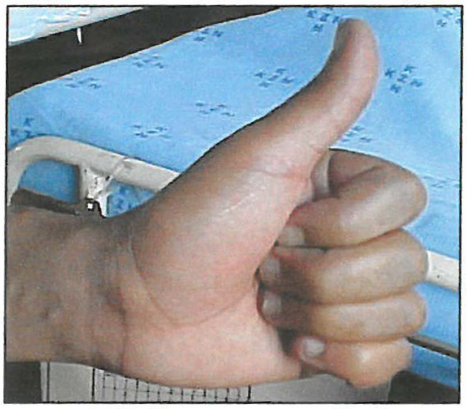


Plate 12 (b): *Effect within 24 hours of thoracoscopic sympathectomy with disappearance of pain and return of hand function*

In contrast, the average inpatient stay following open sympathectomy was 2.5 days. Complications following open sympathectomy included a Horner's Syndrome in 1 patient and wound haematoma in 2 patients.

In all patients the submitted ganglia confirmed the histological presence of neuronal ganglionic tissue.

4.1.3 RAYNAUD'S DISEASE

Thoracoscopic sympathectomy was undertaken bilaterally in 4 patients and unilaterally in one patient, all with associated finger-tip gangrene. All patients had little response to conservative medical therapy. All 5 patients had obtained relief of pain; in three patients, bilaterally, there was healing of the gangrenous tips noted within 6 months of the procedure (Plate 13 a, b). Two patients were lost to follow-up; however, in both these patients there was evidence of clinical improvement within four weeks of surgery.

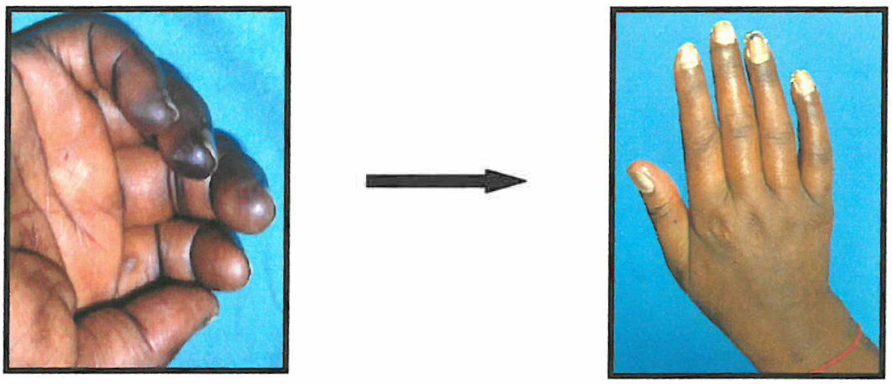


Plate 13 (a) : Raynaud's disease with finger-tip gangrene

Plate 13(b) : Six months following sympathectomy; healing of finger-tip gangrene noted

4.1.4 PERIPHERAL VASCULAR DISEASE

Unilateral thoracoscopic sympathectomy was undertaken in three patients with un-re-constructable upper limb peripheral vascular disease; two of these patients had previously undergone bypass surgery for lower limb peripheral vascular disease. All three patients presented with rest pain; one patient required digit amputation. Following sympathectomy two patients experienced satisfactory pain relief that persisted up to three months following the procedure. The third patient did not obtain any benefit from sympathectomy. All patients were lost to longer term follow-up.

4.2 ISSUES IN TECHNIQUE

4.2.1 OPEN VERSUS THORACOSCOPIC SYMPATHECTOMY

Between December 1994 and March 1995, 20 patients who underwent thoracoscopic sympathectomy were evaluated (Group I). There were 15 females. The mean age of Group I was 19.2 years (range : 13-28). Group II (open sympathectomy) comprised 20 patients; 12 were females. The mean age of Group II was 19.4 years (range : 12-32). This group of patients had their surgical procedures performed during the period August 1992 to July 1993. Forty procedures were performed in each group. The mean operating time for Group I patients was 19 (range :11-30) minutes. In Group II patients, the mean operating time was 87.3 (range : 42-120) minutes.

TABLE 10 : *RESULTS : OPEN VS THORACOSCOPIC SYMPATHECTOMY*

	GROUP I (RANGE)	GROUP II (RANGE)	*p value*
Operating time (min)	19 (11-30)	87.3 (42-120)	*< 0.05*
Hospital stay (days)	1	2.6 (2-5)	
Opioid usage No. of patients Doses	 5 (25%) 1	 20 (100%) 3 (2-11)	*< 0.05*
Return to activity (days)	5 (3-7)	10 (7-18)	*<0.05*

All patients had a successful outcome immediately following surgery that was maintained at the one month follow- up review. All histological evaluation confirmed the presence of neural ganglion tissue. The only complication encountered in each group was a pneumothorax; this was evident in 1 patient in Group I and 4 patients in Group II. This was not statistically significant. Opioid usage was evaluated and only 5 patients in Group I required opioids following surgery as opposed to all the patients in Group II. The number of doses required to sustain pain relief was 3 times greater than that of Group II. Both achieved statistical significance. The hospital stay in Group I was significantly shorter with all but 2 patients being discharged within 24 hours (1-3 days). In Group II the average hospital stay was 2.6 days (2-5 days); this also achieved statistical significance.

All patients in Group I were able to resume their duties by the end of the first week following surgery (mean : 5 days; range : 3-7 days). The mean return to work in Group II was 10 days (range : 7-18 days) with at least 25% only being able to resume normal duties in the third week following surgery. This was statistically significant.

An evaluation of the cost implications of the two approaches demonstrated a significant saving with the patient undergoing thoracoscopic sympathectomy (Table 11). A net

saving of R 4859.40 (R5262.40 if no assistant surgeon is used) is possible for a patient undergoing thoracoscopic sympathectomy.

TABLE 11 : *COST ANALYSIS (IN RANDS) : OPEN VERSUS THORACOSCOPIC SYMPATHECTOMY*

	OPEN	THORACOSCOPIC
Theatre charge*	3238.40	915.00
Theatre consumables	800.00	800.00
Hospital stay♦	2160.00	437.00
Anaesthetic fee	1200.00	760.00
Surgeon's fee	1340.00	1810.00
Assistant's fee	446.00	603.00
TOTAL	**R 9184.40**	**R 4325.00** **R 3722.00 •**

* Standard rate is R35.20 per minute

♦ R720 per day for inpatient; R437 for day case admission

• If no assistant is used

4.2.2 ANESTHETIC CONSIDERATIONS : SINGLE LUMEN ENDO-TRACHEAL INTUBATION VE3RSUS DOUBLE LUMEN ENDOBRONCHIAL INTUBATION FOR THORACOSCOPIC SYMPATHECTOMY

Twenty patients were prospectively evaluated. Group I (double lumen endobronchial, n=10) had a mean age of 18 (15-28) years, weight of 54 (39-71) kg and comprised 4 females. Group II (single lumen endotracheal, n=10) patients had a mean age of 17.5 (16-30) years, weight of 52 (38-68) kg and there were 5 females. There was no statistical difference between the two groups with respect to age, weight and gender distribution.

Desaturation was only encountered in Group I and there were five episodes recorded that was statistically significant ($p< 0.002$). In addition, more supplementary opioids were required by patients in Group I; this was also statistically significant (6 years 1; $p< 0.03$). Pain scores using a visual analogue scale were similar at 2 and 6 hours following the procedure. Retro-sternal discomfort was common and present in both groups (60%) (Appendix 3).

No complications were encountered in both groups.

All patients were discharged within 24 hours.

A successful surgical outcome was achieved in both groups.

sympathectomy. Complications were essentially minor. There was no incidence of a Horner's Syndrome or gustatory sweating. One patient developed a haemothorax that warranted intercostal tube drainage and a hospital stay of three days. A second patient developed surgical emphysema along the right chest wall; chest radiography revealed a small pneumothorax that was managed conservatively over 2 days. The remaining 53 were discharged within 24 hours.

There was an excellent outcome in the immediate post-operative period in all 55 patients with palmar hyperhidrosis; the mean (SD) post-operative score was 0.55 (0.46). This was statistically significant ($p = < 0.0001$). An excellent outcome was also noted in 26 patients (81%) with axillary hyperhidrosis and in 26 patients (53%) with plantar hyperhidrosis.

A satisfactory outcome was volunteered by 3 patients with axillary hyperhidrosis and by 20 patients with plantar hyperhidrosis. There was a poor outcome in 3 patients with axillary hyperhidrosis and 3 patients with plantar hyperhidrosis.

The mean overall (SD) improvement in axillary hyperhidrosis from 7.26 (2.16) to3.14 (2.33) was noted to be significant ($p = < 0.001$); likewise, the mean improvement in plantar hyperhidrosis from 7.32 (2.27) to 3.08 (2.05) was noted to be significant ($p = < 0.001$) (Table 13 and 14).

TABLE 13 : OUTCOME TO LIMITED GANGLIONECTOMY: MEAN (SD) POST OPERATIVE SCORES

	Excellent n (%)	Satisfactory n (%)	Poor n (%)	Mean(SD)
Palmar	55(100)	-	-	0.55 (0.46)
Axillary	26(81.2)	3(9.4)	3(9.4)	3.14 (2.33)
Plantar	26(53)	20(40.8)	3(6.2)	3.08 (2.05)

TABLE 14 : OUTCOME TO LIMITED GANGLIONECTOMY : MEAN (SD) PRE-OPERATIVE VERSUS POST-OPERATIVE SCORES

	Pre-operative	Post-operative	p value
Palmar	9.29 (0.68)	0.55 (0.46)	< 0.0001
Axillary	7.26 (2.16)	3.14 (2.33)	< 0.001
Plantar	7.32 (2.27)	3.08 (2.05)	< 0.001

All patients were extremely gratified with the cosmetic outcome of the procedure. Compensatory hyperhidrosis was by far the most severe side effect and was noted in 7 patients (13%) with a mean LAS score of 7.5 (2.1). This sweating was unpredictable and invariably along the trunks, back and thighs. It usually presented approximately three to six weeks after the procedure. All 7 patients were severely distressed by this side- effect; 3 patients regretted having undergone the operation even though the palms were now dry. Amongst these 7 patients there were 3 patients with axillary hyperhidrosis and 2 patients with plantar hyperhidrosis; there was no change in the sweating patterns in these areas. In 4 patients the compensatory hyperhidrosis was moderate (mean score 4.5); all 4 patients accepted this side-effect and, given the successful outcome of the palmar hyperhidrosis, were satisfied with the outcome.

There was a 100% follow-up at the six months with patients either seen personally or telephonically interviewed. At the end of the study (March 1998) there were 41 patients

followed up for > 9 months; in all these patients the effects of the sympathectomy – both positive and negative – proved to be enduring.

4.2.4 OUTCOME TO THORACOSCOPIC SYMPATHECTOMY : MECHANISMS FOR FAILURE

A total of 448 patients with palmar hyperhidrosis were considered for thoracoscopic sympathectomy : a total of 884 procedures were undertaken. In 12 patients the procedure was undertaken unilaterally. In 6 of these patients, unilateral procedures were performed owing to the presence of dense pleural adhesions that precluded an adequate thoracoscopy. The other 6 patients had unilateral failures (n=4) and recurrent sympathetic activity (n=2).

Progress and outcome in those patients who had not presented for review at 1 week following surgery was established by telephonic contact with patients or the referral doctor. The outcome at 1 week in all patients was known. However, follow-up at 3 months and subsequently was less rewarding with 89% presenting for review or being contactable at one year following the procedure. Follow-up in our practice, which largely subserves a working class population, is notoriously poor; we do, however, have an effective self-referral system.

Persistent Sympathetic Activity (pSA)

At the 1 week follow-up visit, there was a 99.7% successful outcome (<3) to the procedure with complete satisfaction noted on linear analogue scale. In 2 patients, unilaterally, the palmar hyperhidrosis was noted to be persistent. Histological evaluation

confirmed the clinical suspicion that a sympathectomy had not been successfully undertaken.

Two other patients, who had undergone sympathectomy by other surgeons, were referred with pSA noted within 1 week of the procedure. The excised tissue, presumed to be sympathetic neural tissue, was not submitted for histological evaluation by the attendant surgeon. In all 4 patients with pSA, the surgeons had reported little technical difficulty in undertaking the procedure.

Recurrent Sympathetic Activity (rSA)

This was encountered in 2 patients. This included a patient previously reported [Singh,1998]. In these patients, progressive and unilateral recurrence of hyperhidrosis was noted some 30 months after a successful bilateral thoracoscopic sympathectomy. At presentation, the affected limb was as hyperhidrotic as the original state.

Management

All 6 patients (4 pSA and 2 rSA) were managed by re-thoracoscopy. Creation of the pneumothorax was surprisingly easy, there being few significant adhesions. In 3 of the 4 patients with pSA it was apparent that the original surgical endeavour was misdirected. Scarring was noted medial to the 2^{nd} and 3^{rd} rib necks. A 2^{nd} thoracic ganglionectomy was performed and histology confirmed the presence of sympathetic ganglion cells.

In the 4^{th} patient, a dense pleural reaction was noted extending from the region of the stellate ganglion to the 3^{rd} rib. Dissection was difficult; neither the stellate ganglion nor

the 2nd intercostal nerve could be convincingly identified. The procedure was abandoned.

In the first patient with rSA, a contemporaneous video recording of the re-thoracoscopic procedure was made. Scarring was evident along the site of the previous sympathectomy. Dissection from the undissected sympathetic chain distally to the superior aspect of the 2nd rib revealed a cord-like structure connecting to the stellate ganglion (Plate 14).

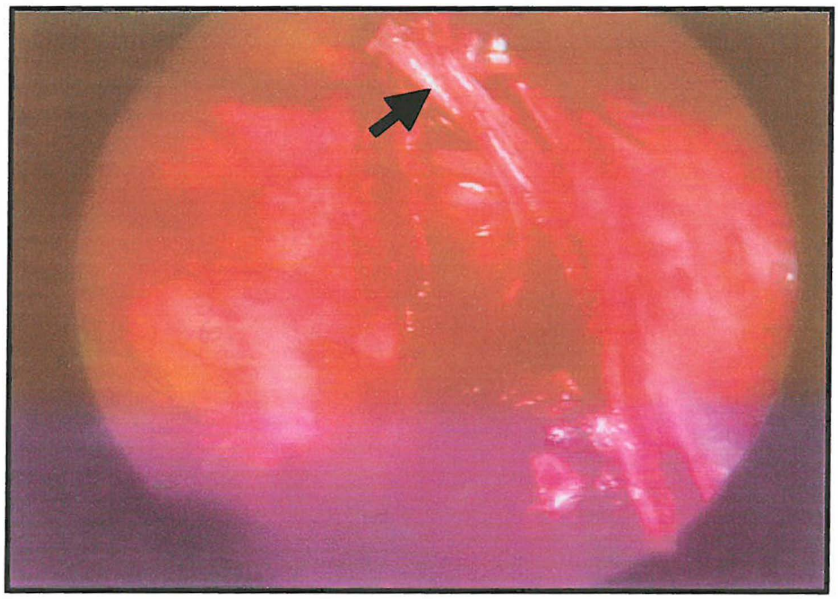


Plate 14 : *Regenerated sympathetic chain (➔) noted at re-thoracoscopy*

Histology of this excised segment revealed haphazardly arranged myelinated and unmyelinated nerve fibers in scar tissue. Axons were noted but no sympathetic ganglia - findings consistent with sympathetic regeneration (Plate 15).

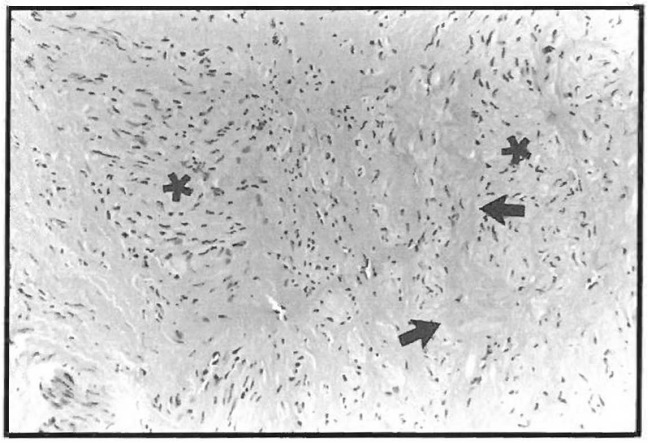


Plate 15 : *Photomicrograph (magnification x 390) illustrating regenerated nerve fibers (asterisk) in scar tissue (arrowed) in patient with recurrent sympathetic activity*

In the second patient with rSA dense scarring was noted along the area of the previously excised 2nd thoracic ganglion; a regenerated sympathetic chain, as described in the first patient with rSA, was not seen. The scar tissue was extensively cauterized; no biopsy could be taken. At 3 months following re-thoracoscopy both patients with rSA showed no signs of recurrent sweating The outcome in the 5 patients subjected to re-thoracoscopic sympathectomy was satisfactory with a mean LAS of 2 noted at the six month follow-up evaluation. To date, this favourable outcome [mean 20.3 (3-60 months)] has persisted.

4.3 ANATOMICAL CONSIDERATIONS

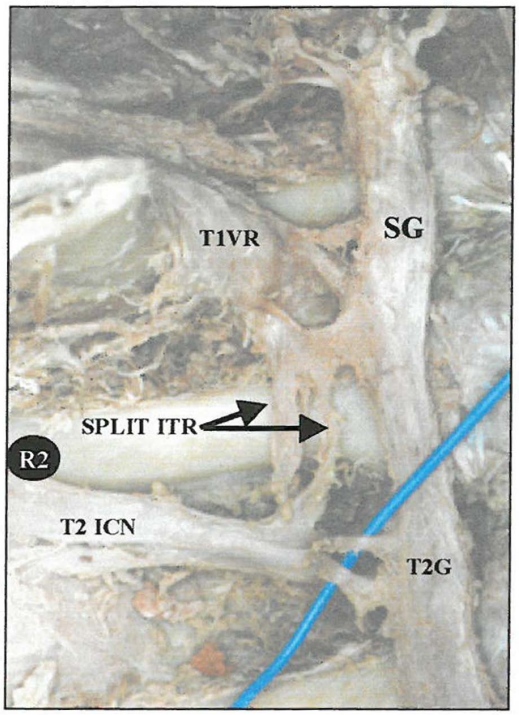
4.3.1 SAMPLE DEMOGRAPHICS

Twenty one cadavers were dissected to define the incidence and location of alternate neural pathways and the morphology of the stellate ganglion. In one cadaver the dissection process was abandoned totally because of chronic lung disease, scarring the thoracic outlet. Thus a total of 41 sides were dissected and were available for evaluation.

4.3.1.1 ALTERNATE NEURAL PATHWAYS

Nineteen out of 21 cadavers (90.5%) demonstrated an alternate neural pathway between the 1st and 2nd thoracic ventral rami. In one cadaver, two alternate neural pathways were noted bilaterally; one cadaver had two neural pathways noted unilaterally.

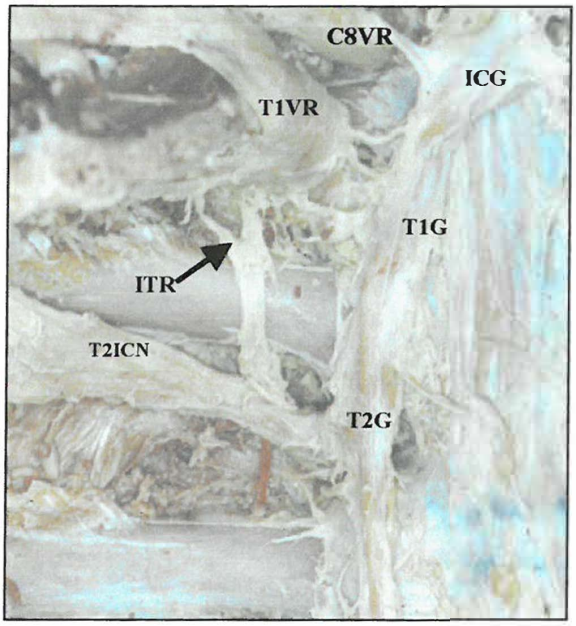
A spectrum of alternate neural pathways were demonstrated. These were categorised as either Type A, Type B or Type C using the intrathoracic ramus (ITR or the nerve of Kuntz) between the 2nd intercostal nerve and the ventral ramus of the 1st thoracic nerve as a basis on both right and left sides (Ramsaroop *et al.*, 2001) (Appendix 4).



TYPE A: This group displayed demonstrable sympathetic connections to either stellate, T2 ganglia or the intergnglionic portion of the sympathetic chain. This was noted in 46.3% ($n=^{19}/_{41}$) (Figure 14, Plate

SG	-	Stellate ganglion
T2G	-	2nd thoracic ganglion
T1VR	-	1st thoracic ventral ramus
ITR	-	Intrathoracic ramus
T2ICN	-	2nd intercostal nerve
R2	-	2nd rib

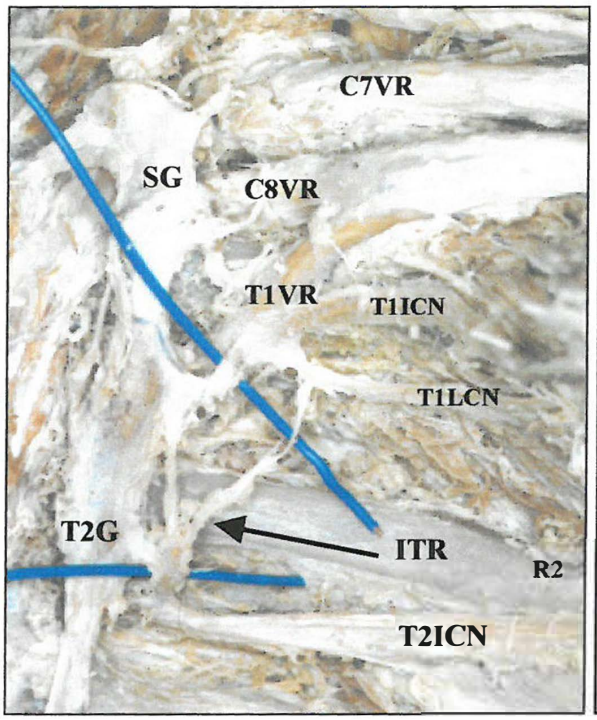
Plate 16 : *Right supero-lateral view demonstrating intrathoracic ramus with macroscopic sympathetic connection (Type A)*



Type B : This group is the classic intrathoracic ramus between the 1st and 2nd thoracic ventral rami. This was noted in 26.8% ($^{11}/_{41}$) (Figure 14,

C8,T1 VR	-	8th cervical, 1st thoracic ventral rami
ICG	-	Inferior cervical ganglion
T1,2G	-	1st, 2nd thoracic ganglia
ITR	-	Intrathoracic ramus

Plate 17 *: Right superolateral view of classic intrathoracic ramus between 1st and 2nd thoracic ventral rami (Type B)*



TYPE C: This group displayed macroscopic sympathetic connections to either the T1 intercostal nerve or its lateral cutaneous branch. This type was noted in 17.1% (n=$^{7}/_{41}$) (Figure 14, Plate 18).

C7,8,T1 VR	-	7th, 8th cervical; 1st thoracic ventral rami
SG	-	Stellate ganglion
T2G	-	2nd thoracic ganglion
T1,2ICN	-	1st, 2nd intercostal nerves
T1LCN	-	lateral cutaneous branch of 1st intercostal nerve
ITR	-	Intrathoracic ramus

Plate 18 : *Left superior oblique view illustrating communication between stellate ganglion and split intrathoracic ramus to lateral cutaneous nerve (Type C)*

Proximity of alternate neural pathways to the sympathetic chain (Appendix 4)

- Mean distance was 10.15mm on the right, range 3.0 - 30.0mm
- Mean distance was 7.18mm on the left, range 2.3 - 12.3mm
- Overall mean distance was 7.66mm, range 2.3 – 30.0mm

Location of 2nd thoracic ganglion and incidence of 2nd ganglion fusion

In the 41 sides analyzed, the 2nd thoracic ganglion was consistently located in the 2nd intercostal space in 37 dissections (90,2%), in 4 dissections (9.8%) the T2 ganglion was noted to be as follows:-

- fused T1 and T2 ganglia lying over the neck of the 2nd rib (2.4%) (Plate 19)

- enlongated, flattened T2 ganglion fused to T1 ganglion and extending to upper border of 3rd rib (2.4%)
- Fused directly to the stellate ganglion (4.8%) (Plate 20)

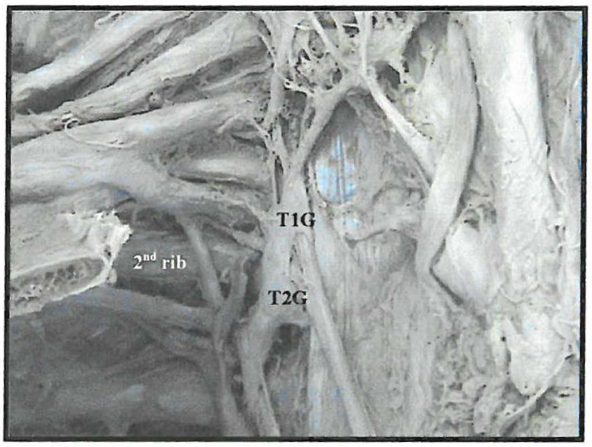


Plate 19 : *Right superior oblique view demonstrating fused T1 and T2 ganglia*

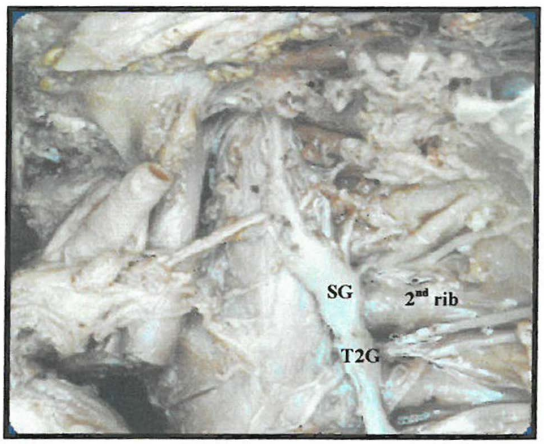


Plate 20 : *Left superior oblique view demonstrating fused stellate and T2 ganglia*

T1G	-	1st thoracic ganglion
T2G	-	2nd thoracic ganglion
SG	-	Stellate ganglion

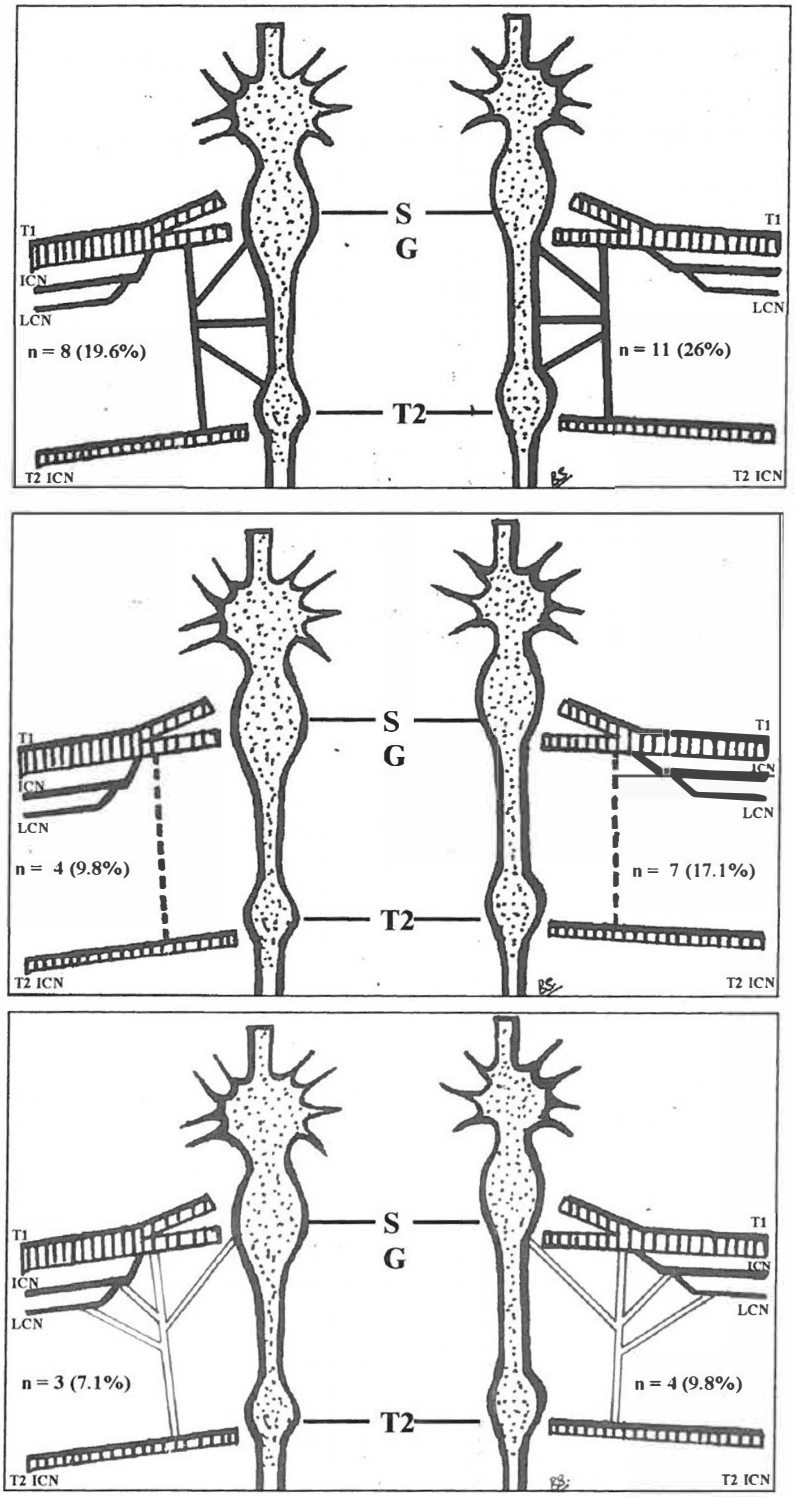


Figure 14 : *Distribution of alternate neural pathways in the 1st intercostal space*

4.3.2 STELLATE GANGLION BLOCK : AN ANATOMICAL RE-APPRAISAL

The sympathetic blockade was undertaken bilaterally in 20 fresh cadavers. The procedure was abandoned on one side because of extensive cervical adenopathy.; a total of 19 blocks were evaluated.

In all 19 blocks, the Toludine Blue Solution consistently tracked posteriorly; there was neither intra-thoracic spillage nor extravasation along the anterior pleura. Proximal spread up to the transverse process of the C7 vertebra was noted in all 19 blocks; this effectively blocked the proximal aspect of the inferior cervical/stellate ganglion. The distal spread extended up to the lower border of the neck of the 3rd rib (n=3), the lower border of the neck of the 4th rib (n=15) and as far as the neck of the 7th rib (n=1). The medial spread was consistently greater than the lateral spread; in all cases the medial spread extended to the medial aspect of the vertebral bodies. The lateral spread in all 19 cases "blocked" the lower roots of the brachial plexus; although alternate neural pathways (Nerve of Kuntz) were not dissected, the lateral spread of the Toludine Blue Solution was consistently noted to be beyond the usual location of the Nerve of Kuntz (Plate 21).

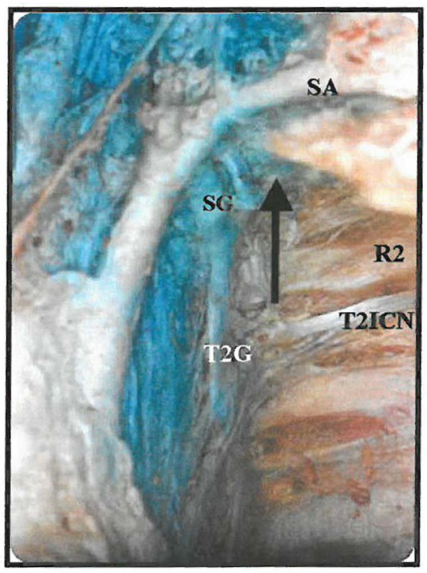


Plate 21 : *Stellate Ganglion Block using Toludine Blue. Note extravasation of dye in the region of the lower trunk of the brachial plexus (→) and the caudal extent of the sympathetic chain*

SA	-	Subclavian Artery
SG	-	Stellate Ganglion
R2	-	2nd rib
T2ICN	-	2nd intercostal nerve
T2G	-	2nd thoracic ganglion

4.4 PATHOLOGICAL CONSIDERATIONS

Control ganglia

In all the control ganglia evaluated no cell surface markers were noted (Appendix 5).

Primary Hyperhidrosis ganglia

All markers that were evaluated were present. This was statistically significant for CD3, CD20, CD4, and CD8. Markers for acute inflammatory cells such as CD68, and LA were present but were not statistically significant (Table 15). The inflammatory response induced a consistent fibrotic reaction in all ganglia.

TABLE 15 : *PRIMARY HYPERHIDROSIS : TEST STATISTICS*[b]

	CD3	CD20	CD4	CD8	CD68	LCA	FIBROSIS
Mann-Whitney U	.000	2.500	5.000	.000	10.000	.000	.000
Wilcoxon W	15.000	17.500	20.000	15.000	25.000	15.000	15.000
Z	-3.075	-2.776	-2.492	-3.068	-1.945	-3.068	-3.606
Asymp. Sig (2-tailed)	.002	.006	.013	.002	.052	.002	.000
Exact Sig [2*(1-tailed)]	.001[a]	.004[a]	.019[a]	.001[a]	.112[a]	.001[a]	.001[a]

a. not corrected for ties
b. grouping variable : ganglion source

CRPS ganglia : surface markers evaluated were present. In these ganglia both the lymphocyte markers, CD3, CD20, CD4 and CD8 as well as the macrophage markers were present in statistically significant amounts. Additionally, the accompanying fibrosis was also statistically significant in the ganglia excised from the patients with CRPS.

TABLE 16 *:CHRONIC REGIONAL PAIN SYNDROME: TEST STATISTICS*[b]

	CD3	CD20	CD4	CD8	CD68	LCA	FIBROSIS
Mann-Whitney U	.000	.000	.000	.000	2.500	.000	7.500
Wilcoxon W	15.000	15.000	15.000	15.000	17.500	15.000	22.500
Z	-3.072	-3.100	-3.072	-3.072	-2.792	-3.068	-2.327
Asymp. Sig (2-tailed)	.002	.002	.002	.002	.005	.002	0.020
Exact Sig [2*(1-tailed)]	.001[a]	.001[a]	.001[a]	.001[a]	.004[a]	.001[a]	.042[a]

a. not corrected for ties
b. grouping variable : ganglion source

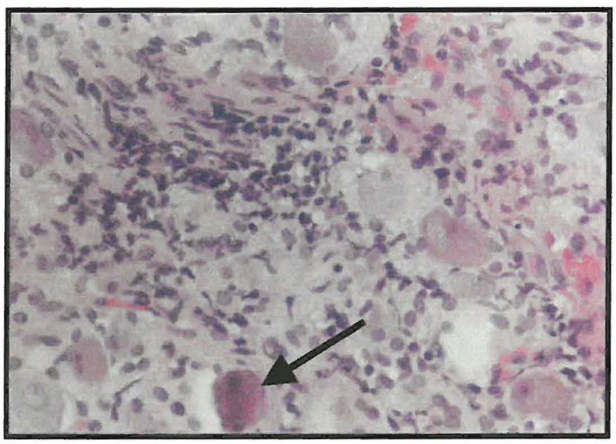


Plate 22 *: Lymphocytic infiltration of sympathetic ganglion with destruction of neurons and associated cytoplasmic condensation (arrow) [Haemotoxylin & Eosin x 180]*

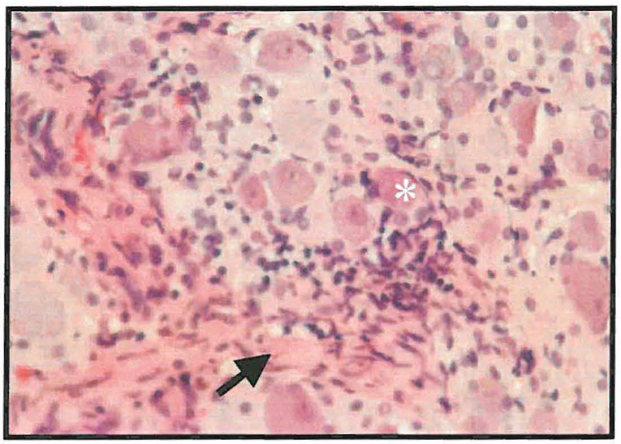


Plate 23 *: Lymphocytic infiltration of sympathetic ganglion with destruction of neurons : Note fibrosis (arrow) and cell destruction (asterisk) [Haemotoxylin & Eosin x 180]*

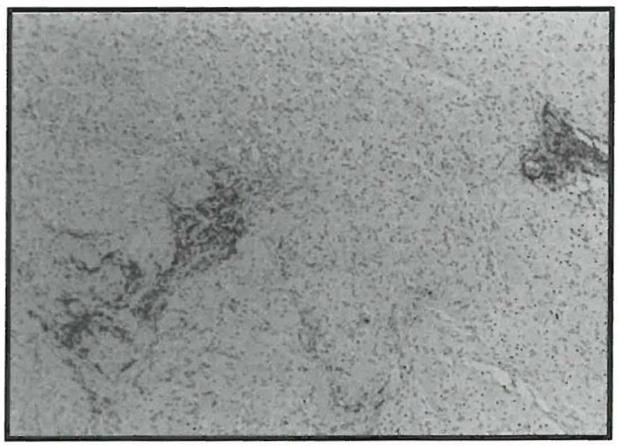


Plate 24 *: Lymphocyte common antigen demonstration of lymphoid aggregates [x 120]*

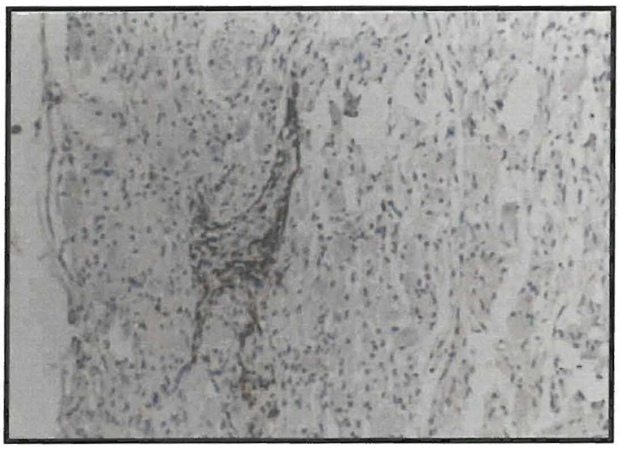


Plate 25 *: CD3 antigen immuno-positivity confirming T-lymphocyte subtype [x240]*

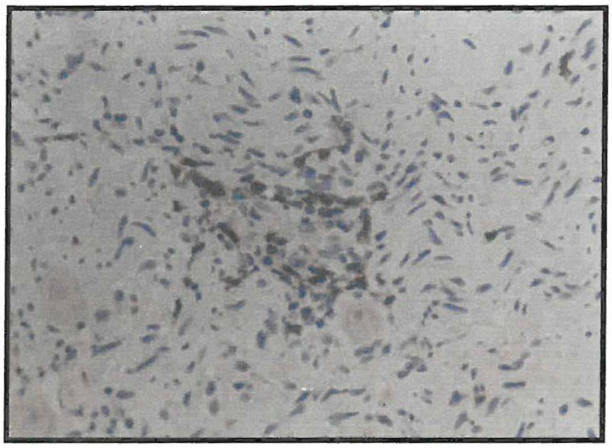


Plate 26 *: CD8 antigen immuno-positivity in lymphoid aggregate [x480]*

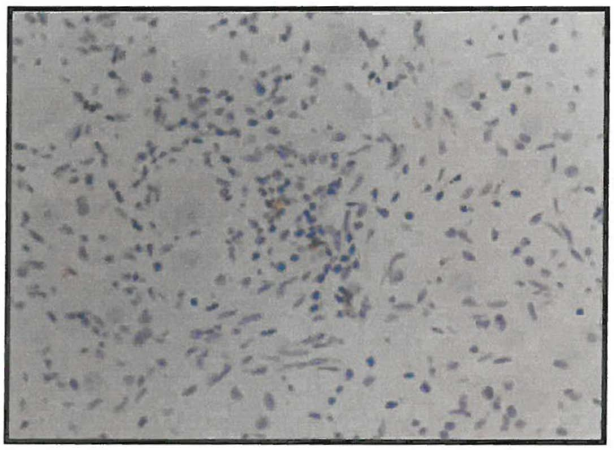


Plate 27 *: Sparse CD4 antigen immuno-positivity in lymphoid aggregate [x280]*

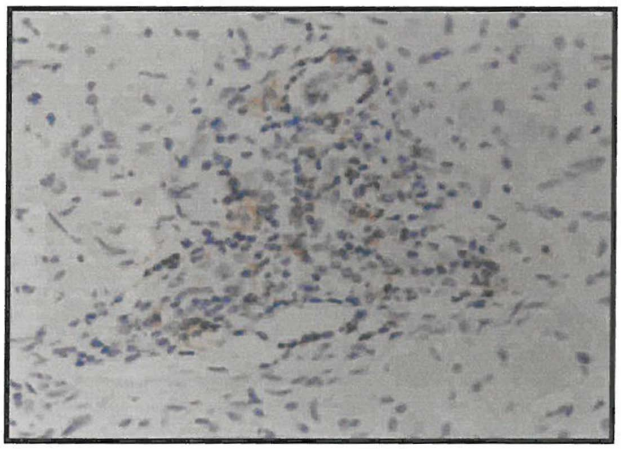


Plate 28 *: Scattered CD20 immuno-positive B lympocyte in lymphoid aggregate*

CHAPTER 5

DISCUSSION

5.1 CLINICAL PERSPECTIVES

Current clinical experience underscores the view that sympathectomy is a relevant surgical option with clearly defined indications. Primary hyperhidrosis is by the most popular indication for sympathectomy; CRPS, in the era of minimal access surgery, has increasingly gained popularity over traditional conservative therapy. Advances in pharmacotherapy and the availability and refinements in vascular techniques have relegated the role of sympathectomy in vasculopathies and occlusive vascular diseases.

5.1.1 PALMAR HYPERHIDROSIS

Since Kotzareff's (1920) somewhat fortuitous treatment of palmar hyperhidrosis by sympathectomy (stellatectomy), surgery has proved to be the most effective and enduring treatment of this condition. Notwithstanding this, various forms of conservative treatment have consistently evolved; this intimates a lingering apprehension about surgery, fuelled probably by the technical demands and complications of open sympathectomy. That no universally safe and easily reproducible open surgical technique is available is reflected by the range of open techniques described. Presently, the wide availability, safety, and reproducibility of the thoracoscopic approach negates the trepidation of surgical risk. The early results of thoracoscopic sympathectomy for upper limb sympathectomy been confirmed in large world wide series (Drott, 1993; Gothberg et al., 1994; Kux, 1978; Lin, 1990). Furthermore, Malone (1986) demonstrated that the technique is easily learnt. When considering surgical management for the treatment of hyperhidrosis, careful patient selection is essential. This entails thorough history taking and clinical evaluation. The clinical picture of primary hyperhidrosis is clear cut, forming a distinct clinical entity. The complaint is invariably of long duration with no change in pattern or influence on

general health. Special investigations are unnecessary, the only tests being done are those necessary to qualify the patient for a general anaesthetic. In this series a pre-operative chest radiograph was not routinely performed; if there was a history of chronic lung disease or pulmonary trauma a chest radiograph was done.

Despite the success of thoracoscopic sympathectomy the search for an appropriate conservative treatment continues, prompted by the occasional unpleasant and unpredictable effect of sympathectomy. Compensatory hyperhidrosis (Chapter 5.2.3) is the foremost of these unpleasant effects and is arguably the major reason for the search for conservative treatment. To date no conservative treatment has been shown to effect the enduring treatment of hyperhidrosis. The injection of Botulinum toxin , the most recently described conservative treatment, is yet to be proved as an effective, economic, and enduring alternative.

Gustatory phenomenon , originally described by Guttmann (1921), developed in one patient. This phenomenon has been described to occur in up to 5% of patients undergoing sympathectomy (Moron and Brady, 1991; Kux,1978). It has been suggested that gustatory sweating represents an expression of aberrant regeneration or collateral sprouting of preganglionic fibers making abnormal synapses in the superior cervical ganglion (Kurchin et al., 1977a). The low incidence of this effect in this series endorses the suggestion that it may be obviated by confining the sympathectomy to the 2nd thoracic ganglion.

In this series a Horner's syndrome (with ptosis, meiosis and rhinitis) developed in one patient; this complication gradually improved over the ensuing six months, not warranting corrective surgery. This complication developed during the early phase of

our experience with thoracoscopic sympathectomy when cautery was applied onto the sympathetic chain prior to its transection. Unipolar cautery applied to the sympathetic chain has the potential to extend proximally (and distally) and thereby lead to unwanted coagulative necrosis. In general, the incidence of Horner's syndrome is related to the approach used; for cervical sympathectomy the reported incidence ranges from zero (Bogokowsky et al., 1983) to 40% (Adar et al., 1977). Horner's syndrome was not observed in 2 series that used the transaxillary approach (Ellis 1975; Sternberg et al., 1982), in several series that used the endoscopic route (Kux, 1978; Malone et al., 1982; Byrne et al., 1990) and in the largest in the literature that used the dorsal midline approach (Shih and Wang ,1978). The thoracoscopic approach affords the easy recognition of the stellate ganglion (by its characteristic overlying yellow fat pad) so that its injury is avoided. In those rare instances (<1%) of 1st and 2nd thoracic ganglion fusion it is suggested that the sympathectomy be confined to below the lower border of the 2nd rib; at this level the innervations to the 1st thoracic ganglion and inferior cervical ganglion (to eyelid) are intact.

Phantom sweating ie the subjective feeling of impending sweating in the palms without actual sweating has been reported in a high percentage of patients (Hashmonai et al., 1992 ; Adar et al.,1977; Kurchin et al., 1977b). Many series, including this, do not mention this effect. It is conceivable that detailed questioning of the patient may probably elicit this effect.

Transient palmar sweating appearing 1 to 7 days after successful sympathectomy (that was followed by complete anhidrosis) is disconcerting to the patient and the surgeon. This occurred in three patients in this series and has also been reported by others (Adar

et al., 1977; Greenhalgh et al., 1971; Keaveny, 1977). The reason for this phenomenon is unclear; it has been suggested that it may represent a transient discharge of the neurotransmitter substance at the nerve ending resulting from post-ganglionic degeneration. If the surgeon is confronted by this phenomenon after a technically successful sympathectomy, the patient should be reassured about the long-term effect. In contrast to transient hyperhidrosis, recurrence of hyperhidrosis in the long-term may be due to nerve regeneration. The incidence of recurrent hyperhidrosis ranges between 1 to 5%, occurring between 2 to 48 months following sympathectomy (Hashmonai et al., 1992). In this series relapse of hyperhidrosis – as opposed to persistent sympathetic function – occurred in 2 of 884 limbs that were noted to anhidrotic following sympathectomy.

Post sympathectomy rhinitis, has been reported to occur in 3.5 to 10% of patients (Hashmonai et al., 1992; Herbst et al., 1994); this side-effect was not volunteered by any patients in this study. In the report by Hashmonai et al. (1994) and Herbst et al. (1994), T1/T2 – T4 and T1-T4 components of the sympathetic chain were resected. It has been speculated that post-sympathectic rhinitis follows the diminished sympathetic but increased parasympathetic stimulation of nasal mucosa leading to nasal obstruction because of mucosal oedema (Whittet and Fisher, 1988).

No long term respiratory complaints were volunteered by any patients in this series ; Herbst et al. (1994) and Hashmonai et al. (1992) also did not report respiratory problems following sympathectomy. However, Adar et al., (1977) and Adar (1994) reported the persistence of respiratory complaints beyond the post-operative period in patients returning to physical activity. This was substantiated by Molho et al. (1980)

who demonstrated a change in pulmonary function following sympathectomy. For three to six months after surgery, pneumo-constriction and a small increase in airway resistance was demonstrated; subsequently the pulmonary function normalized. Adar et al. (1977) also reported in his series of 100 patients the re-exacerbation of childhood bronchial asthma (in 2 patients) and the cessation of asthma attacks (in 1 patient). The basis for the improvement of asthma following sympathectomy is not known.

Most of the hyperhidrosis series deal with the adult population; in this series the mean age at surgery was 19.2 years (range 13-52 years), although most had been affected since early childhood. Similarly in Sternberg's series (1982) the mean age operated upon was 22,5 years; 10 to 15 years of conservative treatment elapsed before surgery was performed. Shih and Wang (1978) in his series of 457 patients reported that 91% had symptoms dating from childhood but surgery was only performed between the age 21 to 25 years. The situation is similar in many other series (Gruszkiewicz et al., 1986; Adar et al., 1977; Gjerris and Olsen, 1975; Gothberg et al., 1994). Apprehension to outcome to open sympathectomy and the belief in conservative therapy by the attendant physician are the reasons for the belated referral of children for sympathectomy. However, there have been reports of successful sympathectomy in children. Rode et al. (1986) reported a good outcome in his series of 14 transaxillary sympathectomies undertaken in children with an average age of 9 years. O'Donoghue et al. (1980) reported on 4 children (aged between 6–13 years, symptoms commencing at 2 years) subjected to supraclavicular sympathectomy ; outcome was good, although one child developed a transient Horner's syndrome . Mares et al. (1994) in his series of 67 patients (mean age 14 years, range 5.5 to 17 years), reported that there was a successful outcome to transaxillary sympathectomy in all but 2 patients. In the light of

the reported successful outcome to open sympathectomy in children, should thoracoscopic sympathectomy be offered more widely in this population group? The effects on pulmonary physiology following insufflation during thoracoscopy in children are not fully appreciated. Furthermore, crucial in the selection of patients is the degree of debility and the extent of the hyperhidrosis i.e. regional versus generalized. It is a moot point whether a child less than 14 years could be capable of quantifying these issues. An unanswered question is whether hyperhidrosis spontaneously regresses; if this happens, sympathectomy in a sub-set of patients may be an unnecessary procedure. For these reasons it is suggested that sympathectomy be deferred until adolescence when the scholastic and social restraints posed by hyperhidrosis become quantifiable.

The development of cardiac arrhythmias during thoracoscopic sympathectomy is an uncommon, potentially lethal side-effect rarely described. Lin et al. (1994) who undertook thoracoscopic sympathectomy from the left side initially, reported 2 cases of cardiac arrest preceded by arrhythmias. In this series, 2 patients who developed severe bradycardia had the sympathectomy initially undertaken on the left side, contrary to our standard practice; both patients reverted to sinus rhythm spontaneously on stopping further manipulation of the sympathetic chain. The mechanisms responsible for arrhythmias during sympathectomy are not known. This effect was not reported during the era of open sympathectomy when cautery was rarely applied on the sympathetic chain. The minimal amount of current necessary for inducing ventricular fibrillation is lower for the left stellate ganglion than for the right stellate ganglion. Thus, less stimulation to the left stellate ganglion is needed to produce an arrhythmia compared to the right stellate ganglion (Armour et al., 1972; Hagemann et al., 1973, Schwartz, 1973). The left sympathetic chain and vagus nerve innervate the atrio-ventricular node;

the right sympathetic chain and vagus nerve innervate the sino-atrial node, the principal pacemaker. When the sympathectomy commences on the right side, the sino-atrial node is able to adapt to the changes prompted by the sympathetic manipulation (and accommodates further manipulations on the left sympathetic chain). By contrast, when the left sympathetic chain is manipulated initially, the atrio-ventricular node is unable to handle manipulations and traction on the sympathetic chain and becomes out of sync with the sino-atrial node, leading to arrhythmias. In addition to starting on the right side there should be minimal manipulation and traction on the sympathetic chain; on freeing the overlying pleura, the sympathetic should be transected initially between the T1-T2 ganglion before proceeding to further manipulations.

Haemothorax developed in one patient; this patient had pleural adhesions, the freeing of which was thought to cause the haemothorax. Bleeding at thoracoscopic sympathectomy is usually minor, self limiting and usually follows injury to the intercostal veins; the superior intercostal vein may be located anterior or posterior to the sympathetic chain (on the right side) may be a source of troublesome bleeding. If the dissection is adjacent to and confined to the sympathetic chain, injury to the underlying intercostal artery could be avoided.

Pneumothorax following thoracoscopic sympathectomy is usually the result of the failure to fully evacuate the pleural space by suction and application of positive end expiratory pressure; the herniation of lung up to the intercostal muscles following the latter maneuver should always be sought out for. Lung injury (at the time of Veress needle or trocar placement) is uncommon and is reflected by the rapidity of the resolution of the pneumothorax (within 12 to 24 hours in this series). The need to

routinely undertake a post-operative chest radiograph is a moot point; a residual pneumothorax probably exists in large proportion of patients but is not clinically significant.

In the minimal access era, sympathectomy for hyperhidrosis has been consistently described as a relatively minor procedure well received by patients and associated with excellent results and few complications. The Achilles heel of this procedure remains compensatory hyperhidrosis. It is this effect that courts objection to surgical intervention for what is a benign functional disorder. Indiscriminate surgery for all patients presenting with hyperhidrosis should be discouraged. Careful patient selection is crucial with patients being fully informed of the spectrum of possible side effects.

5.1.2 CHRONIC REGIONAL PAIN SYNDROME

Even though various theories have been proposed (Doupe et al., 1944; Livingstone, 1943; Melzack and Wall, 1968) for the pathophysiology of CRPS, this condition remains poorly understood; it is hardly surprising that there is not a uniform approach to therapy. Functional restoration of the affected limb can only be established by relief of pain. This encourages movement, prevents contractures, maintains limb function, reduces vascular stasis and prevents osteoporosis. The analgesic modalities available include pharmacological agents, regional anaesthesia or neuromodulation (Raj and Wilder, 1995). The sequence of application of these modalities varies from center to center, depending on the personal experience and the expertise of the attendant physician. The preferred therapy has little scientific basis (Ochoa, 1995). There is, however, unanimity that CRPS may progress from an acute, to a dystrophic and then to an atrophic stage (Drucker et al., 1959). Each clinical stage may last from several weeks

to months. The acute phase may be considered as being reversible and resolution is possible with medical therapy. A good result may also be anticipated when the analgesia provided by regional sympathetic or stellate ganglion blockade extends beyond the duration of the block itself. Whilst SGB might prove useful as a therapeutic modality, it was shown to be a poor predictor of outcome to surgical sympathectomy in this series.

The dystrophic phase usually has a poor response to stellate or regional blockade. Spontaneous resolution is uncommon. The atrophic stage represents the final and unforgiving phase of CRPS that is usually unresponsive to therapy (Mockus et al., 1987). This temporal progression of CRPS may have therapeutic implications. In choosing the appropriate therapeutic algorithm it is imperative that it is time contingent. Early recognition during the acute phase stage is crucial as it may readily afford a favourable outcome following either drug therapy or sympathectomy. The mainstay of an early diagnosis is clinical awareness. Laboratory, radiological, histological and neurophysiological studies have little value in this regard (Schott, 1995). The failure to promptly recognise and appropriately treat CRPS may result in a complicated clinical course with irreversible changes, as well as a missed opportunity for relief by sympatholytics or sympathectomy.

The range of pharmocotherapeutic options advocated includes non-steroidal anti-inflammatory agents, corticosteroids, biphosphonates, calcitonin, anti-depressants, anti-convulsants, opioids and, sympatholytic drugs (Raj and Wilder, 1995). Amongst the latter are oral agents (phenoxybenzamine) and transdermal agents (clonidine) (Byas-Smith et al., 1995). These agents are prescribed in combination and may have disconcerting side effects and underscore the failure of a suitable pharmacological

option. In concert with medical treatment, physiotherapy and occupational therapy are crucial in expediting functional restoration. Given the complexity of the condition and its management, it is advisable that a multidisciplinary team affiliated to a pain clinic manages these patients. This affords access to pharmacologists, anaesthetists, physiotherapists, physicians and surgeons, each of whom may have a role to play. Compensation neurosis is an under-appreciated factor in these patients; the role of a psychologist, occupational therapist and a welfare agency early in the management may be of salutary benefit (Raj and Wilder, 1995; Raj et al., 1990).

SGB is undertaken in our practice when, at the end of 6 weeks, medical treatment proves to be ineffectual. SGB may be both diagnostic and therapeutic. It has been suggested that if performed accurately, sympathetic blockade may define the so-called Sympathetic Mediated Pain (SMP), thereby justifying the role of sympathectomy. Furthermore, if undertaken in the early or acute phase, the procedure may prove to be therapeutic in itself (Mokus et al., 1987; Abu Rahma et al., 1994). However, the drawbacks to SGB are manifold; the procedure is operator dependant and its universal accuracy unknown. Furthermore, the stellate ganglion is distant from the 2nd thoracic ganglion that is now considered pivotal in effecting upper limb sympathetic denervation. Also, alternate neural pathways to the brachial plexus bypass the stellate ganglion and may not be blocked by a standard SGB. Thus, SBG may under-estimate the true incidence of SMP and thereby deny patients a potentially beneficial outcome from sympathectomy. In the present series, a beneficial outcome was noted in 20 of 25 patients identified by sympathetic blockade as having sympathetic mediated pain and in 15 of 17 patients with a poor response. Thus, contrary to the experience of others (Mockus et al., 1987; Abu Rahma et al., 1994) the response to sympathectomy did not

correlate with the response to SGB. Open sympathectomy was required in 2 of 24 patients (8.4%) in group 1 patients and was required in 10 of 18 patients (55.5%) in group 2 patients. Since there was no antecedent history of pulmonary infection or chest trauma, these adhesions and pleural thickening obscuring the sympathetic chain were considered to be a consequence of SGB.

Three months from the onset of symptoms was the arbitrary period chosen to distinguish early from late onset CRPS as by that stage standard therapy becomes largely ineffectual. Clinical assessment of response to therapy by a consistent medical team is important. Persistence of a conservative approach does not guarantee spontaneous resolution of symptoms and this has to be balanced against the prospect of progress to the dystrophic stage that is disastrous for most patients, particularly manual labourers.

Spurling (1930) originally described sympathectomy as an effective treatment for CRPS when he successfully treated a patient (then described as having causalgia) by performing a stellate ganglionectomy. Since then, the value of sympathectomy, particularly when undertaken timeously, has been endorsed by others (Mockus et al., 1987; Abu Rahma et al., 1994; Thompson, 1979). However the role of sympathectomy has been a controversial issue (Ochoa, 1995; Schott, 1995; Schott, 1998). Our study demonstrates that all patients referred timeously (within 3 months) for sympathectomy, have an excellent or good result. When sympathectomy is undertaken beyond this stage, a favourable outcome is not guaranteed and only 8 of 18 patients (44.4%) had a good or excellent outcome. Overall, sympathectomy was noted to have a good or excellent outcome in 32 (76.2%) of our patients. The results in this series and the range of available therapies suggest that a placebo-controlled trial may not be feasible or indeed

ethical. The role of sympathectomy in current practice is enhanced by the ease and safety of the thoracoscopic approach (Byrne et al., 1990; Hsu et al., 1994; Singh et al., 1996).

In this study, thoracoscopic sympathectomy has been shown to be a safe option with a better outcome than in those patients undergoing open surgery. Results in the latter category of patients were adversely influenced by the longer duration of symptoms. The greater number of SGB undertaken in this group may have contributed to apical thickening and adhesions that precluded thoracoscopic sympathectomy and thereby the benefit of a minimally invasive procedure. Early clinical recognition without persistent SGB affords the opportunity of successfully accomplishing thoracoscopic sympathectomy, an option that may be invaluable in the management of CRPS.

An understanding to the mechanisms of the sympathetic pathway is useful to the understanding of the anatomical basis that makes sympathectomy effective, particularly for the treatment of CRPS. Figure 15 (Pick, 1970) is the standard depiction of autonomic reflex pathway. In general the autonomic nervous system does not include nerve components which conduct impulses into the central nervous system. The afferent neurons which conduct impulses from visceral organs to the spinal cord and the brain stem are visceral afferent components of the spinal and cranial nerves. The cell bodies of these neurones , like those of the somatic afferent neurones, are located in the ganglia associated with the sensory roots of the respective nerves.

Both visceral and somatic afferent nerve fibers make reflex connections with pre-ganglionic neurons in the spinal cord and the brain stem. They are, therefore,

functionally related to the autonomic nerves , but are not anatomic components of them. The simplest autonomic reflex arc consists of an afferent conductor (either visceral or somatic), a connecting mechanism located to the central nervous system and an efferent conducting chain made up of a pre-ganglionic and a ganglionic neuron. It is the interruption of the reflex arc at the ganglionic level that makes sympathectomy an effective option for conditions such as CRPS. The interruption of the reflex arc along the afferent pathway is impractical; in contrast, a ganglionectomy has no deleterious effect on somatic nervous function. Figure 16 provides the anatomical rationale for a ganglionectomy However, this arrangement has not been scientifically verified. The histological demonstration of sympathetic collateral nerve sproutings in the dorsal root ganglion and the presence of inflammatory cells in the sympathetic ganglia excised from patients with CRPS, suggests that the afferent pathway may extend, in the first instance, to the nearest ganglion i.e. sympathetic ganglion. The ulnar and median nerves are the principal source of sympathetic neurones among the peripheral nerves. The pathway is then to the dorsal root ganglion. Interruption of the pathway at the level of the 2^{nd} thoracic ganglion therefore provides an afferent and efferent blockade.

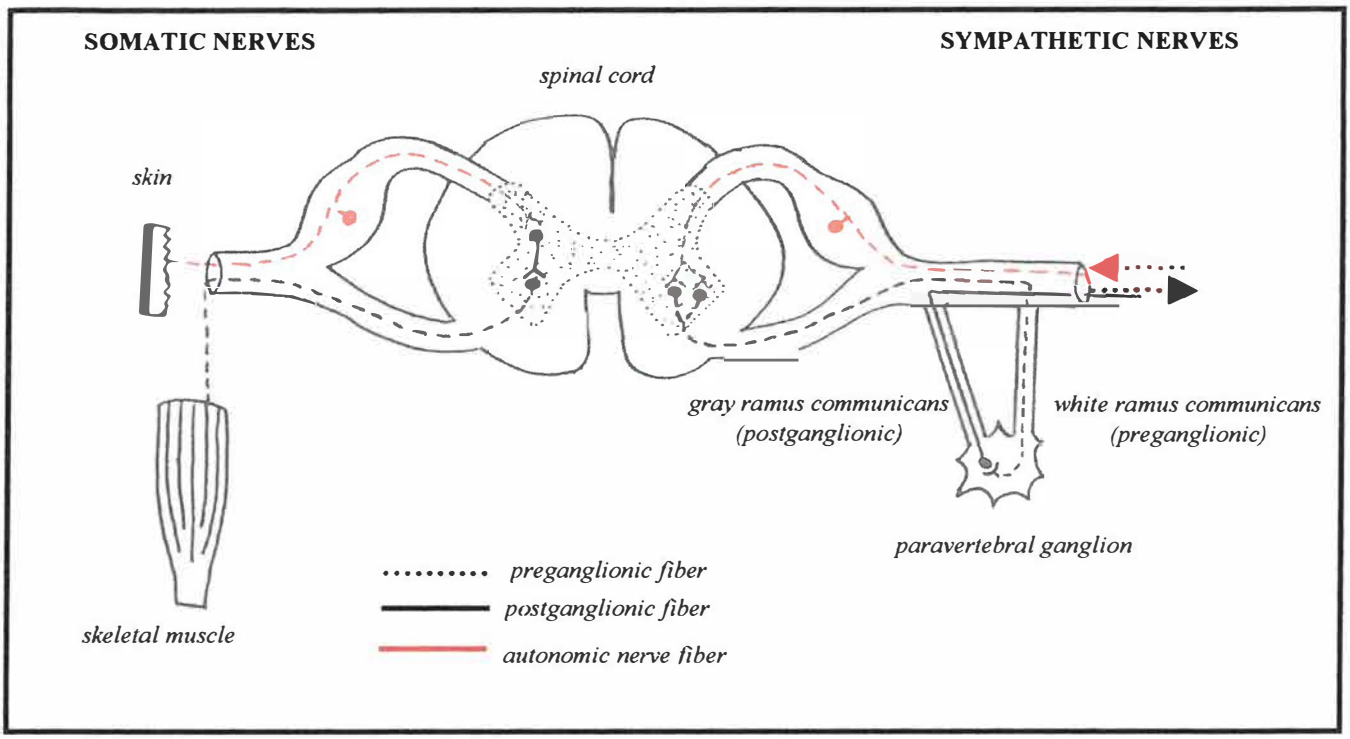


Figure 15 : *The principle of the sympathetic outflow from the spinal cord and of the course and distribution of sympathetic fibers*

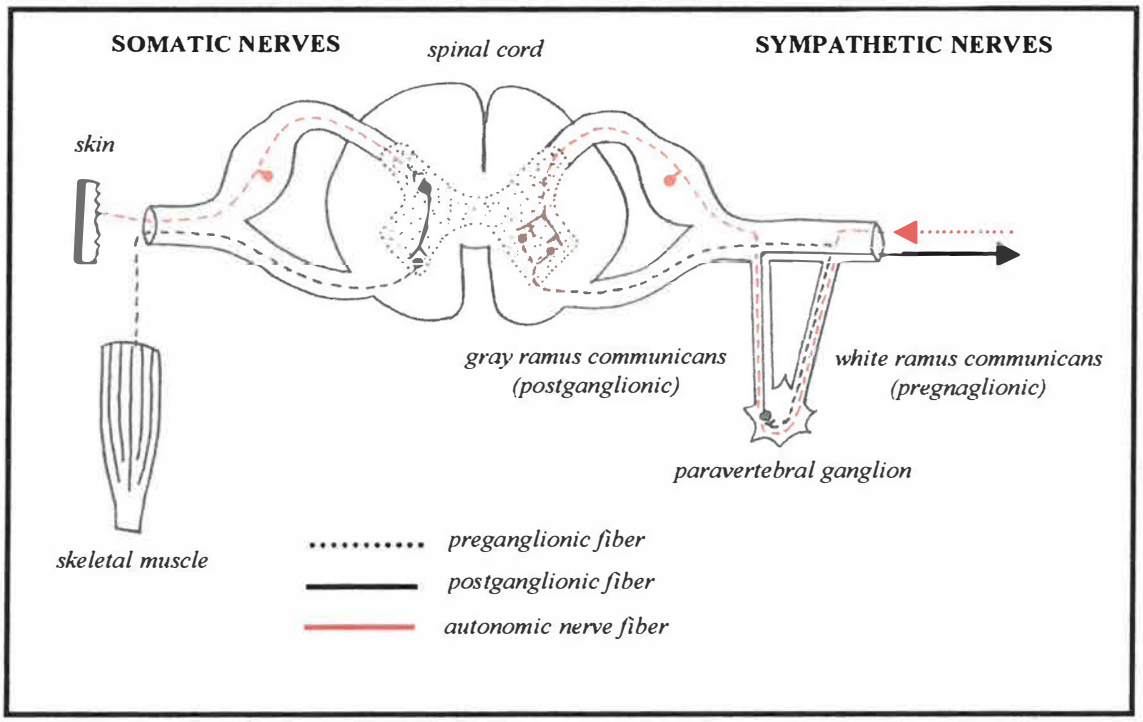


Figure 16 : *Postulated sympathetic afferent pathway that may provide an anatomical basis for ganglionectomy in chronic pain syndromes*

The effectiveness of the 2nd thoracic ganglionectomy implies that the upper limb sympathetic outflow is via this ganglion. The middle and stellate (inferior cervical and 1st thoracic ganglion) do not have pre-ganglionic contributions; thus, the persistence of middle cervical and stellate ganglionic function following 2nd thoracic ganglionectomy suggests that the pre-ganglionic contributions to the 2nd thoracic ganglion (the highest level of pre-ganglionic spinal outflow) must ascend to the middle and stellate ganglia. This would explain the avoidance of a Horner's Syndrome. It also underscores the anatomical significance of the 2nd thoracic ganglion for upper limb sympathetic supply. An extrapolation of this view is that the spinal sympathetic segments are not synonymous with ganglionic levels – the highest spinal segment (T1) issuing pre-ganglionic fibers to the 2nd thoracic ganglion.

5.1.3 RAYNAUD'S DISEASE

The low incidence of sympathectomy undertaken in this series for vascular disease is representative of current surgical opinion. This follows the unpredictable and invariably disappointing outcome following open sympathectomy (Birnstingl, 1967; Landry *et al.*, 1996); the ease and safety of thoracoscopic sympathectomy may prompt a re-think on this issue (Baker et al., 1994 ; Milewski et al., 1985.). Presently the guidelines are unclear since the value of thoracoscopic sympathectomy has largely come in the form of case reports and uncontrolled studies (Claes et al., 1994 ; Baker et al., 1994). Furthermore, channel blocking agents may be of value in some patients with Raynaud's disease, a condition which has shown the tendency to resolve spontaneously on occasions (Gordan et al., 1994).

Raynaud's disease infrequently gives rise to serious complications. Although patients may symptomatically improve in the short term there is a tendency for the condition to recur in the long-term (Montorsi et al., 1980 ; Johnstone et al., 1965). Gifford et al., (1958) concluded that no definite advantage could be attributed to sympathectomy over medical treatment. Providing that sympathectomy can be undertaken with minimal morbidity and mortality it is a reasonable treatment option for the severe manifestations of the condition such as digital gangrene as demonstrated in the five patients treated in this study. A relative indication is the persistence of symptoms notwithstanding optimal medical treatment.

5.1.4 PERIPHERAL VASCULAR DISEASE

In a small number of patients with severe upper limb ischaemia reconstructive vascular surgery will not be feasible. In this category of vascular patients the ease and safety of thorascopic sympathectomy may be a reasonable option to improve rest pain and defer or even avoid amputation. The role of sympathectomy in these patients is largely based on the management of lower limb non-reconstructible vascular disease ; the role of sympathectomy for upper limb vascular disease is therefore extrapolated from that experience. In general, the outcome to sympathectomy is difficult to interpret because of poor patient selection and definition and the absence of prospective, randomized evaluation. Furthermore, as in this experience, the long term outcome is not stated.

Thus, Repelaar van Driel (1988) reported that at 6 months 14% of patients with rest pain and 45% with gangrene required major amputation. Gordan et al. (1994) and Barnes (1994) suggested that there was circumstantial evidence that sympathectomy may be effective in those patient with rest pain who stop smoking. Johnson (1998), in reviewing the outcome to lumbar sympathectomy in 29 patients with focal necrosis with a long term follow-up in 10 patients, suggested this approach may be useful in a sub-set of patients (ABI > 0.03, with transcutaneous oxygen tensions less than 30mmHg that increase more than 20mmHg with limb dependency).

Notwithstanding the absence of controlled, randomized trials to validate its role and in the absence of alternative therapy, thoracoscopic sympathetectomy may have an increasingly important role to play in the management of this difficult and uncommon

problem; in this review was shown to be useful (in the short-term) in two of the three patients in whom it was undertaken.

5.2 ISSUES IN TECHNIQUE

5.2.1 OPEN VERSUS THORACOSCOPIC SYMPATHECTOMY

The thoracoscopic approach has been convincingly shown to be superior to the standard supraclavicular approach in terms of technical requirements and cost saving to the patient. Although patient evaluation of these procedures was not undertaken it is apparent from the opioid usage, hospital stay and the cost benefit that the thoracoscopic approach will be considered to be superior. The prospect of tiny scars compared to the much larger supraclavicular scars of the open procedure will undoubtedly also make the thoracoscopic approach more favourable. Given the longstanding satisfactory experience with thoracoscopic sympathectomy for palmar hyperhidrosis, it would be difficult to undertake a prospective randomized study comparing this approach with the open approach. This study was prompted by the comparative study of the short term results of open supraclavicular sympathectomy and thoracoscopic sympathectomy of the 2^{nd} to 4^{th} thoracic ganglia in two randomly selected groups of 12 patients with palmar hyperhidrosis reported by Hashmonai et al., (1994); in this study though dry hands were achieved in all patients, patients in the thoracscopic group had a longer anaesthetic time and were less satisfied one week after surgery. Hashmonai (1994) concluded that the supraclavicular sympathectomy did not take longer, was no more difficult than thoracoscopic sympathectomy and might be associated with less morbidity and greater subject satisfaction. These results, reported in 1994, were probably

reflective of the early experience with thoracoscopic sympathectomy. In 1996, the same group reported 106 thoracoscopic sympathectomies in 53 patients with palmar hyperhidrosis; all limbs were dry at the end of the procedure and at a mean follow-up of 19.5 months 88.5% of the patients had expressed subjective satisfaction prompting the authors to conclude that thoracoscopic sympathectomy was preferred to open sympathectomy in the management of palmar hyperhidrosis (Kopelman et al., 1996).

Support for the thoracoscopic approach (over the open trans-axillary approach) has also been provided by Yilmaz et al. (1996). While both procedures were equally effective, there was less post-operative pain, shorter hospital stay and more rapid recovery following thoracoscopic sympathectomy.

The longer operating time for supraclavicular open sympathectomy in this study (mean : 92 minutes; range : 42-130 minutes) is reflective of the technical challenge sometimes presented by this approach. In our practice, the open technique is undertaken by an experienced surgeon, assisted by a surgeon of comparable experience. By contrast, thoracoscopic sympathectomy may be undertaken safely and quickly (in our experience mean operating time : 19 minutes; range : 11-30 minutes) by surgeons equipped with basic minimal access surgical skills. Our experience suggests that the technique may be undertaken without an assistant surgeon. The solitary surgeon undertakes the procedures using a two-handed technique (one hand camera, one hand for surgery). The latter approach has a cost saving implication.

Whilst no surgical procedure is free from complications, the relative ease of undertaking sympathectomy safely via the thoracoscopic route firmly establishes this as the

approach of choice for upper limb sympathectomy. Basic minimal access techniques and a sound appreciation of the thoracoscopic anatomy of the sympathetic chain are necessary caveats.

5.2.2 ANAESTHETIC CONSIDERATIONS : SINGLE LUMEN ENDO-TRACHEAL INTUBATION VERSUS DOUBLE LUMEN ENDOBRONCHIAL INTUBATION FOR THORACOSCOPIC SYMPATHECTOMY

Most published articles stress the importance of lung isolation with a double-lumen endobronchial tube (DLEBT), paralysis and controlled one lung ventilation for thoracoscopic sympathectomy (Banker et al., 1993; Miller et al., 1992).

The value of single-lumen endotracheal (SLET) intubation for thoracoscopic sympathectomy has been demonstrated by Lee (1994). SLET was shown to be safe, economic and did not compromise the thoracoscopic approach (Marshall and Marshall, 1980). Nothwithstanding these advantages, a comparison of SLET with DLEBT intubation anesthetic technique (with respect to effects on SaO_2, hypoxis and pain) has not been previously undertaken. This study, in addition to confirming the study of Lee et al., (1994) has demonstrated that SLET is associated with less post-operative opioid requirement. Retro-sternal chest pain was the major reason for the administration of opioids and the prolongation of the hospital stay. The SLET technique was shown to be a simpler technique that obviated the need for the more expensive and more difficult to place DLEBT. Unlike the technique described by Lee (1994), following the partial collapse of the lung caused by disconnecting the SLET tube from the anaesthetic circuit, the pneumothorax is sustained by the insufflation of carbon dioxide. A pneumothorax no more than 5cm (from the apex of the thorax) is all that is required for the procedure.

A larger collapse of the lung (>70%) may cause the protective effect of hypoxic pulmonary vasoconstriction to be abolished; partial lung collapse to the degree described with or without carbon dioxide insufflation does not decrease the hypoxic pulmonary vasoconstriction. Blood is therefore directed to better ventilated areas, thereby safely maintaining SaO_2 levels. Total lung collapse is likely to follow DLEBT, predisposing to the loss of the protective effects of hypoxic pulmonary vasoconstriction (Marshall and Marshall, 1980).

When applying carbon dioxide insufflation this should not be rapid; rapid carbon dioxide insufflation may lead to tension pneumothorax, displacement of the mediastinum and possibly haemodynamic instability. During insufflation accidental lung puncture (by Veress needle or trocar) may result in sudden steep increase in end tidal carbon dioxide concentration which is evident by a classic wave form on the capnograph. Irrespective of the technique used, insufflation of no more than 0.8 litres of carbon dioxide is usually sufficient for a safe procedure. The advantage of carbon dioxide insufflation is the fairly rapid development of the pneumothorax; with the opening of the inserted cannula to atmospheric pressure, the lung may take up to fifteen minutes to collapse (Grichnik et al., 1993; Robinson et al., 1994). To sustain the partial lung collapse the anesthetist should ensure that positive end expiratory pressure is not applied because this will prevent lung deflation. Notwithstanding these concerns, the overall safety of SLET for a procedure that is short (<20 minutes) in patients who are usually young and fit, lends this procedure to be taken as a same day case. Although not evaluated in this study subsequent experience suggests that SLET allows for thoracoscopic sympathectomy to be undertaken as a same day case.

The feasibility of undertaking thoracoscopic sympathectomy using a SLET technique represents a transformation in anaesthetic practice. From the initial practice of DLEBT with carbon dioxide insufflation (Jedeiken et al., 1992) this was modified to the use of DLEBT without carbon dioxide insufflation (Robinson et al., 1994). The use of SLET with insufflation represents what should be standard practice in the anaesthesia for thoracoscopic sympathectomy. The major advantages of SLET is elimination of the complications associated with DLEBT, notwithstanding the improved design of double lumen tubes. Furthermore, 38-83% of DLEBTs are found to be malpositioned when evaluated with fiber-optic bronchoscopy. Thus, it has been suggested that positioning of the double lumen tubes should always be confirmed by bronchoscopy (Hurford and Alfille, 1993). This may have further technical and cost implications with the possible prolongation of the anaesthetic time. The SLET technique does not require the use of a bronchoscope and the intubation is therefore quicker and simpler. The advantages of SLET are listed in Table 17.

***TABLE 17** : ADVANTAGES OF SINGLE LUMEN INTUBATION*

1. Avoids problems of DLEBT insertion • Malposition • Less traumatic to airway than DLEBT • Expensive DLEBT avoided
2. Avoids problems associated with the IPPV* of one lung ventilation • Potential rupture of the subpleural blebs • Potential loss of ability to ventilate with bilateral air leaks
3. Possibly better V/Q matching with spontaneous ventilation
4. Possibly less shunt to collapsed lung with spontaneous ventilation

* = *Intermittent Positive Pressure Ventilation*

The SLET technique may be unsuitable in patients who have an absolute indication for DLEBT, for example, when there is the potential for spillage of infected sputum or if conversion to an open thoracotomy is contemplated. These are however, uncommon clinical scenarios since patients presenting with thoracoscopic sympathectomy are invariably fit and usually without the history of lung disease. In the latter situation the more appropriate approach would be an open sympathectomy via the supraclavicular approach. This study has shown that the SLET technique with insufflation is associated with fewer episodes of desaturation and less need for opioid analgesia compared with DLEBT. Furthermore, hypotensive episodes were not recorded and the surgical exposure not compromised by the SLET technique.

5.2.3 LIMITED GANGLIONECTOMY : A PROSPECTIVE EVALUATION

Primary hyperhidrosis, particularly of the palms, causes much psychosocial trauma and sometimes physical discomfort; on occasions this condition may compromise an individuals vocation. It is therefore not surprising that the palmar component of primary hyperhidrosis is what drives the patient to seek treatment. By contrast axillary hyperhidrosis, even though it occurred in just under 60% of our patients, was rarely troublesome to the extent that specific treatment was requested. Likewise plantar hyperhidrosis – evident in nearly 90% of our patients – was largely tolerable, even though longstanding plantar hyperhidrosis predisposes to blistering, infections, bromhidrosis and rotting of shoes and socks (Moran and Brady, 1991).

Surgical sympathectomy, by various approaches, has long been acknowledged as offering the most effective and enduring treatment of hyperhidrosis.

Minimal Access Surgery, using the thoracoscopic approach, has gone a long way to diminishing the morbidity associated with open sympathectomy (Byrne et al., 1990; Kux, 1978; Singh et al., 1996; Edmonson et al., 1991). Notwithstanding this, there are two problems associated with sympathectomy undertaken for hyperhidrosis that persists during the thoracoscopic era. These relate to the problem of compensatory hyperhidrosis and the appropriate management of axillary hyperhidrosis. We suggest that these issues are related to the extent of the sympathectomy undertaken for upper limb hyperhidrosis.

Compensatory hyperhidrosis is recognized as an unpredictable but potentially devastating effect of thoracic sympathectomy. The reported incidence of compensatory hyperhidrosis ranges from 22-81% (O'Riordain et al., 1993; Hsu et al., 1994). This wide range probably reflects the varying extent of the sympathectomy undertaken for upper limb hyperhidrosis. In addition most series fail to quantify the degree or severity of the compensatory hyperhidrosis.

The mechanisms responsible for compensatory hyperhidrosis are unclear. Whereas the original hyperhidrotic state may be induced by emotions, amongst other factors, compensatory hyperhidrosis tends to be largely a heat regulated phenomenon. Following upper limb sympathectomy nearly 40% of the total sweat gland function is lost; it is therefore not surprising that the residual truncal sweat glands show unusually increased activity, thereby producing compensatory hyperhidrosis. Thus, the greater the

number of sweat glands excluded from thermoregulatory control, the greater the chance of compensatory hyperhidrosis. However, other factors may yet be involved because compensatory hyperhidrosis may occur even in an air-conditioned environment (Shelley and Florence, 1960; Andrews and Rennie, 1997).

The surgical technique of clipping the sympathetic chain and removing these clips on the development of compensatory hyperhidrosis is an interesting option that merits further evaluation. The preliminary results reported by Lin (1998) suggests that this approach may prove to be invaluable in the management of this difficult problem.

Notwithstanding this, reducing the extent of the sympathetic ganglionectomy has been associated with a lower incidence of compensatory hyperhidrosis. An incidence of compensatory hyperhidrosis of up to 64% has been reported when the ganglionectomy is extended up to the 5^{th} or 6^{th} thoracic ganglion. By contrast, limiting the extent of the ganglionectomy to the 2^{nd} thoracic ganglion has been associated with a reduction in compensatory hyperhidrosis to between 22 – 24%. Hederman (1994) has reported a 24% incidence with electrocautery of the 2^{nd} thoracic ganglion. O'Riordain (1993) has reported a 22% incidence of compensatory hyperhidrosis following precise excision from below the stellate ganglion to above the 3^{rd} ganglion, effectively removing the 2^{nd} ganglion and the adjacent interganglionic segment. The anatomical basis for a successful upper limb sympathectomy with a 2^{nd} thoracic ganglionectomy was described by Hyndman and Wolkin, but clearly was not widely appreciated (Hyndman and Wolkin, 1942).

In this series the overall compensatory hyperhidrosis rate is 20% (11 patients); if the 4 patients assessed to have moderate, tolerable compensatory hyperhidrosis are excluded that rate of severe compensatory hyperhidrosis is 12.6% (7 patients).

Assessment of compensatory hyperhidrosis is based on subjectivity, rather than on objective sweat production analysis. It is suggested that compensatory hyperhidrosis rates may be significantly reduced by a meticulous dissection and resection of only the 2nd thoracic ganglion. Diathermy application on the sympathetic chain should be avoided as this may cause a coagulative necrosis proximal and distal to the 2nd thoracic ganglion, thereby effectively extending the extent of the ganglionectomy. For similar reasons traction should not be applied on the chain. These technical considerations are probably the basis for the absence of facial anhidrosis and gustatory sweating in this series.

Accurate localization of the 2nd thoracic ganglion is crucial and is afforded by dissection of the pleura off the chain and a thorough appreciation of the anatomy of the thoracic sympathetic chain. However, compensatory hyperhidrosis remains largely unpredictable; when severe this side-effect surplants the presenting palmar hyperhidrosis. In this series 3 of the 7 patients with severe compensatory hyperhidrosis regretted undergoing the procedure (even though their palms were now anhydrotic). A variety of non-surgical measures such as topical agents (aluminium chloride, tanning agents, glutaraldehyde), iontophoresis (electric coagulation of the eccrine sweat glands) and systemic anticholinergic agents have been used, invariably, without much success. For these reasons it behoves the attendant surgeon to fully counsel the patient about this potential side-effect (Andrews and Rennie, 1997).

Because axillary hyperhidrosis often occurs concomitantly with palmar hyperhidrosis, the traditional approach has been to perform an extended sympathectomy (up to the 5^{th} – 6^{th} thoracic ganglion) in an endeavour to effect axillary anhidrosis. The anatomical basis for this approach is unclear. The potentially devastating effects of an extended sympathectomy have been mentioned; furthermore it has been reported that extensive ganglionectomy does not guarantee a successful outcome for axillary hyperhidrosis (Bretteville, 1973). Clearly a balanced approach is necessary. We suggest that extensive sympathectomy should not be undertaken for concomitant axillary hyperhidrosis, particularly as axillary hyperhidrosis is rarely a presenting factor. Rather, we recommend a limited 2^{nd} thoracic ganglionectomy be offered. This was associated with an 80% success rate for axillary hyperhidrosis and a disabling compensatory hyperhidrosis rate of 12.6% in our series. In those patients troubled with persistent axillary hyperhidrosis excision of the axillary sweat glands is probably the best option. To date none of our patients have qualified for this procedure which entails excision of an ellipse of skin with careful undermining above and below to remove the deeper layer containing the sweat glands. Siting of the incision is important to avoid an unsatisfactory scar that may restrict arm movement following excision (Hurley and Shelley, 1966).

Plantar hyperhidrosis occurred in 49 patients (89%) but was never a prime complaint; the anatomical basis for the successful treatment of plantar hyperhidrosis by 2^{nd} thoracic ganglionic (in over 80% of the patients) is unclear. The successful treatment of plantar hyperhidrosis following thoracic ganglionectomy should be regarded as a bonus and, as such, should not be guaranteed to the patient.

Our experience with this procedure suggests that for primary hyperhidrosis thoracoscopic sympathectomy maybe performed on a day care basis and that a limited 2nd thoracic ganglionectomy is adequate to treat palmar hyperhidrosis. Furthermore, this approach may cure axillary hyperhidrosis and more importantly, decrease the incidence of debilitating compensatory hyperhidrosis.

5.2.4 OUTCOME OF THORACOSCOPY FOR PALMAR HYPERHIDROSIS : MECHANISMS FOR FAILURE

The persistence and recurrence of the sympathetic function following a seemingly successful sympathectomy are often reflective of surgical and anatomical misinterpretation of the sympathetic chain, as well as the ability of the sympathetic chain to regenerate. By contrast, rSA or pSA following successful sympathectomy for vasculopathies, particularly Raynaud's phenomenon, is reflective of the unpredictable responses of these conditions to surgery rather than to the factors cited (Haxton,1947). The role of alternate neural pathways [ANPs], specifically the nerve of Kuntz, an inconstant and variable intrathoracic ramus between the 2nd thoracic intercostal nerve and the T1 root was long considered an important cause of sympathetic reactivity. This was especially emphasized during the era when stellate ganglionectomy was the standard surgical procedure for upper limb sympathectomy (Figure 6). In current surgical practice, wherein the 2nd thoracic ganglionectomy is standard practice, the significance of ANPs is dubious. The 2nd thoracic ganglionectomy effectively interrupts the sympathetic outflow to the upper limb proximal to these ANPs thereby eliminating their surgical significance (Figure 17).

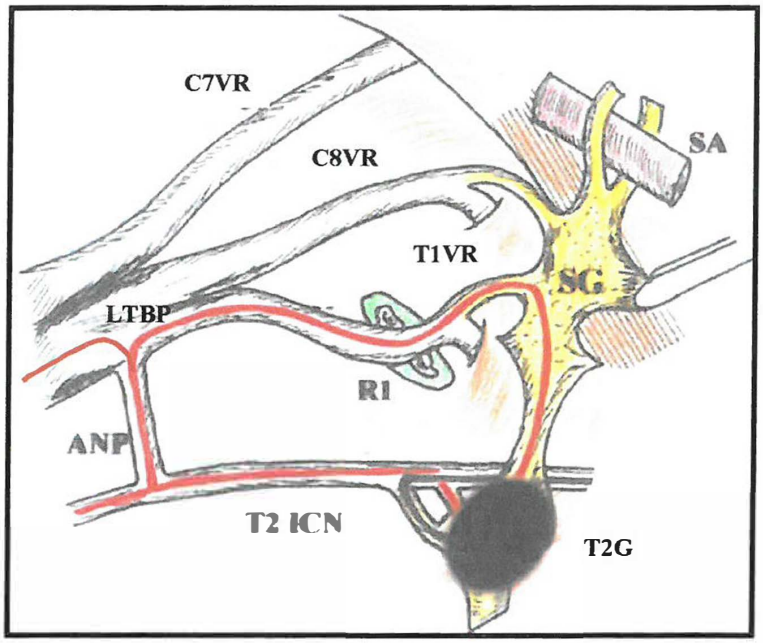


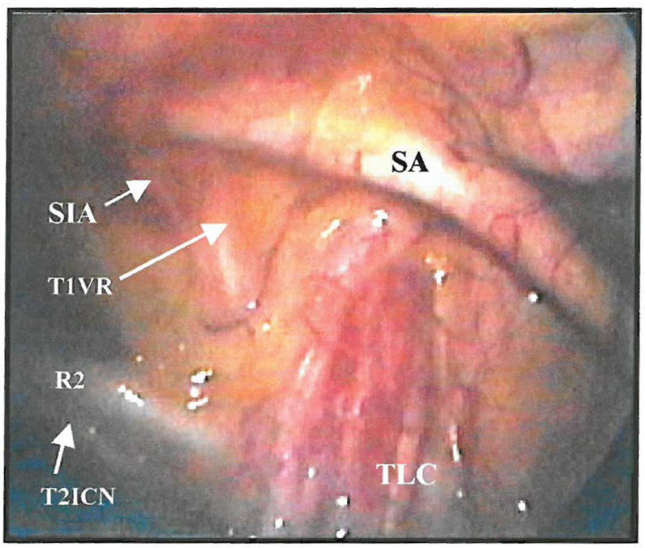
Figure 17 : *T2 ganglionectomy interrupts sympathetic outflow to the brachial plexus notwithstanding the alternate neural pathway (ANP)*

C7,8,T1 VR	-	7^{th}, 8^{th} cervical, 1^{st} thoracic ventral rami
SA	-	Subclavian artery
SG	-	Stellate ganglion
T2G	-	2^{nd} thoracic ganglion
LTBP	-	Lower trunk of brachial plexus
R1	-	1^{st} rib
ANP	-	Alternate neural pathway
T2 ICN	-	2^{nd} intercostal nerve

For most surgeons thoracoscopic sympathectomy is a novel approach. It compels us to consider the probability of misinterpretation of the anatomy as an important cause of persistent sympathetic function. Furthermore, the teaching of the surgical anatomy of the sympathetic chain and its variations is under-emphasized during standard surgical training. In 3 patients with pSA, it was apparent that the location of the sympathetic

chain was not appreciated at the primary procedure; it is conceivable that this also occurred in the 4th patient. Fibrosis consequent to this intervention precluded a safe re-operation. In such situations, an extensive *en-bloc* excision of the 2nd and 3rd intercostal nerves with their spinal ganglia and surrounding tissue has been suggested as a useful option to be undertaken at open surgery (van Rhede van der Kloot and Jörning, 1990). The authors are not comfortable with undertaking this option thoracoscopically.

Plate 29 demonstrates the potential of the fascia overlying the tendon of longus colli muscle (TLC) being misinterpreted as the sympathetic chain. The TLC lies medial to the sympathetic chain and is a much broader structure. However, with inappropriate dissection, it may easily be mistaken for the sympathetic chain.



SA	-	Subclavian artery
SIA	-	Superior intercostal artery
T1VR	-	1st thoracic ventral ramus
R2	-	2nd rib
T2ICN	-	2nd intercostal nerve

Plate 29 : *Thoracoscopic view of right proximal sympathetic chain; note TLC mimicking the sympathetic chain*

Sympathetic regeneration accounting for rSA has long been a controversial issue; whilst some authors found no evidence of regeneration at re-operation, others (Telford,1935; Jepson, 1951) attributed this phenomenon to rSA (Mattasi et al., 1981; Haxton 1970). However, reports incriminating nerve regeneration have often not been accompanied by the histological evidence of nerve regeneration.

Regenerating nerve fibers establish contact between the divided ends by thin strands that may grow to the caliber of the sympathetic chain. Regeneration is only effective when the connecting neural fibers are correctly aligned. Return of sympathetic activity depends on the extent of the regenerating process and the proportion of sympathetic fibers successfully re-establishing a functional pathway. Conceivably, a greater number of sympathetic re-connections do occur but, because of inappropriate functional connections, returned sympathetic activity is subclinical. The rarity of this phenomenon underscores the difficulty of re-establishing functional sympathetic re-connections (Singh et al., 1998).

Nerve regeneration may be suspected clinically by the gradual return, over months to years, of sympathetic activity to assume the pre-sympathectomy state. This is in contrast to the presence of intact ANPs wherein the surgery does not affect sympathetic activity (Singh et al., 2001).

Failure of effective sympathectomy is uncommon and rSA is even rarer. From the afore-mentioned findings, it is apparent that pSA is invariably a technical misadventure. Circumvention of this pitfall necessitates appreciation of the surgical anatomy of the 2nd thoracic ganglion which is located in the 2nd intercostal space somewhat distal to the

corresponding intercostal nerve and adjacent to the superior border of the 3rd rib. However, this ganglion has been reported to be located anterior to the 3rd rib in 15% of cases (Chiou and Liao, 1996). It is incumbent upon the surgeon to be familiar with the landmarks that assist with its identification. The 2nd intercostal nerve, located medial to the 2nd rib's posterior angle, is an under-appreciated landmark that directs to the T2 ganglion. Similarly, the superior intercostal artery (a branch of the costocervical trunk of the subclavian artery), runs an infero-lateral course parallel to the sympathetic chain at an average distance of 10 mm from the sympathetic chain. This artery ends as the 2nd intercostal artery and has been suggested to be a useful landmark (Chiou and Liao, 1996).

Electrophysiological stimulation to confirm the location (and appropriate ganglion level) of the sympathetic chain has been suggested; this expensive, time-consuming and complicated manoeuvre has, unsurprisingly, not gained wide acceptance in surgical practice (Lindquist et al., 1989).

The results presented in this study accurately reflect the outcome to sympathectomy 1 week following the operation; at that visit instances of early failure would have been evident. Less clear is the true incidence of late recurrence since the long-term outcome could not be evaluated in all patients. Given the potential of the sympathetic chain to regenerate, it is a moot point whether the described case in this series is truly reflective of the phenomenon.

Today, the great numbers of thoracoscopic sympathectomies undertaken have re-defined the role of ANPs. Our experience has also demonstrated the need to be

appreciative of the anatomy of the sympathetic chain. Furthermore, instances of rSA and pSA may be safely and readily treated by the thoracoscopic route (Singh et al., 1996).

5.3 ANATOMICAL CONSIDERATIONS

5.3.1 ALTERNATE NEURAL PATHWAYS

The incidence and array of alternate neural pathways associated with the 2nd thoracic ganglion should alert the surgeon to the clinical significance of these. Historically, alternate neural pathways were considered responsible for an unsuccessful sympathectomy. Since Kuntz's original description (Kuntz, 1927), the role of alternate pathways has cast a questioning shadow on the technique of sympathectomy. However, in current practice employing an isolated 2nd thoracic ganglionectomy, this is not the case. An isolated 2nd thoracic ganglionectomy- without addressing alternate neural pathways- has an almost 100% successful outcome in effecting upper limb sympathectomy. What are the reasons for this ?

i. When stellate ganglionectomy was the standard practice, sympathetic outflow from the 2nd thoracic ganglion was unaffected; thus fibres issuing from the 2nd thoracic ganglion- including the alternate neural pathways- may potentially afford an alternate pathway via the T2 ganglion and the alternate neural pathway to the T1 root (Figure 6).

ii. As the surgical practice of sympathectomy evolved from stellate ganglionectomy to 2nd to 4th thoracic ganglionectomy to, as in current practice, a limited T2 ganglionectomy, the clinical significance of alternate neural pathways gradually dissipated. This would suggest, from extrapolation of clinical outcome, that the T2 ganglion is pivotal to upper limb sympathetic innervation. T2 ganglionectomy effects sympathetic denervation at level before the alternate neural pathways become clinically relevant (Figure 17).

iii. Is it conceivable that during the performance of a T2 ganglionectomy, alternate neural pathways are inadvertently removed? In the technique of T2 ganglionectomy described, the surgical dissection is confined to the T2 ganglion, the interganglionic segment and the T2 rami communicantes. Notwithstanding this precise technique-aided by ample illumination and magnification- it is conceivable that alternate neural pathways may be avulsed during this procedure.

In the cadaveric dissections undertaken, the alternate neural pathways, when encountered, were noted to be located at a mean distance of 7.66 (range 2.3-30.0) mm lateral to the sympathetic chain along the inferior border of the 2nd rib. Given the 7-fold optical magnification afforded by thoracoscopy, it is surprising that alternate neural pathways are not readily encountered when the dissection is confined to the T2 ganglion. It is a moot point whether these alternate neural pathways are located far laterally, out of the magnified operating field. However, when looked for, alternate neural pathways will be noted (Plate 30).

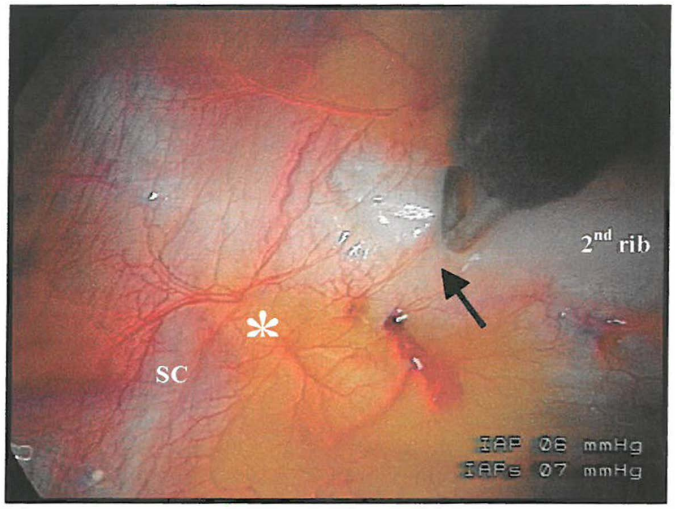


Plate 30 : *Left thoracoscopic sympathectomy : transpleural view of alternate neural pathway (Nerve of Kuntz) indicated by arrow*

SC	-	Sympathetic chain
*	-	Location of 2nd thoracic ganglion

If alternate neural pathways need to be defined, our technique is to commence dissection medial to the sympathetic chain in the region of the 2nd intercostal space (rather than over the 2nd rib) (Plate 24).

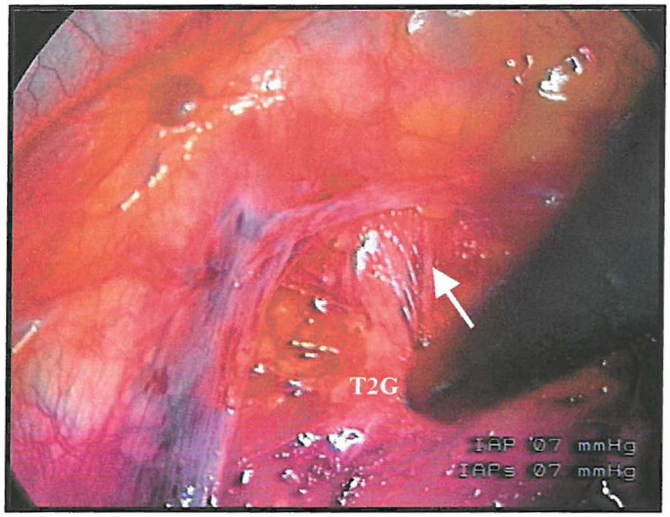


Plate 31 : *Left thoracoscopic sympathectomy : alternate neural pathway (Nerve of Kuntz, indicated by arrow) demonstrated after dissection of pleura*

T2G	-	2nd thoracic ganglion

What is the significance of alternate neural pathways in current surgical practice? Our current understanding suggests that the superior spinal outflow (by white rami communicantes) is to the stellate ganglion. The persistence of the middle and superior cervical ganglion function (given that there is no white rami to these) suggests that the white rami to the stellate ganglion must ascend to the middle and superior cervical ganglia. The avoidance of a Horner's effect and a facial anhidrosis by undertaking a T2 ganglionectomy further emphasizes the role of the T2 ganglion (and its white ramus) in effecting upper limb sympathetic function. Extirpation of the T2 ganglion would interrupt the sympathetic outflow proximal to the stellate ganglion and the brachial

plexus; outflow to the T2 root would also be interrupted as would the alternate neural pathways that issue from it.

Thus, whilst the alternate neural pathways have long held interest as an important cause of an unsuccessful sympathectomy, in the context of the current practice of a 2nd thoracic ganglionectomy they hold no surgical significance. Certainly, as demonstrated during the era of stellate ganglionectomy, these alternate neural pathways were significant. Following stellate ganglionectomy, they afforded a pathway from the intact 2nd thoracic ganglion to the T2 root and, when present, via alternate neural pathways to the T1 root (and thereby to the brachial plexus).

In the era of 2nd thoracic ganglionectomy, it is not surprising that surgeons rarely appreciate alternate neural pathways. It has been noted that these are rarely encountered when the sympathetic chain is dissected thoracoscopically and that the clinical outcome (following 2nd thoracic ganglionectomy) is excellent. Furthermore, many surgeons prefer to cauterize the sympathetic chain, thereby having an even smaller opportunity to visualize alternate neural pathways.

Further definitions of the sympathetic chain and its variations add to the body knowledge of the sympathetic nervous system. The anatomy of the sympathetic nervous system has long been unchallenged. Anatomical detail in many current texts have been largely unchallenged and unchanged over the past century. With the increasing numbers of sympathectomies been undertaken- largely afforded by its ease when undertaken by the minimally invasive route- a wider clinical appreciation of this operation may further evolve. Thus, a greater understanding of the anatomical vagaries

will prove invaluable in further refining established surgical techniques and approaches. A case in point is the role of the Stellate Ganglion Block (SGB) in predicting the response to sympathectomy in patients with CRPS involving the upper limb. The development of a Horner's Syndrome following SGB has long been considered to also reflect a sympathetic blockade of the ipsilateral upper limb; improvement of the CRPS following SGB, in current practice; suggests that the pain is "sympathetic maintained" qualifying the patient for a sympathectomy. In the light of our present understanding of sympathetic pathways to the upper limb, correlated by clinical experience with a 2nd thoracic ganglionectomy, it is apparent that SGB may not consistently provide an upper limb sympathetic blockade. To effect an accurate sympathetic blockade of the upper limb, it is necessary to block the 2nd thoracic ganglion. Thus a SGB, in patients with CRPS, may not truly reflect those patients who would benefit from a sympathectomy. It is conceivable, however, that injectate may infiltrate down (from the region of the SGB) to the 2nd thoracic ganglion, thereby accounting for a proportion of patients who would qualify for sympathectomy. It is therefore appropriate to challenge the technique and status of the SGB vis-à-vis its role in the management of CRPS given the anatomical considerations outlined.

Notwithstanding the peripheral role of alternate neural pathways in upper limb sympathectomy, the original descriptions of these by Albert Kuntz (in 1927) will long continue to engender anatomical interest. The spectrum of alternate neural pathways following Kuntz's description of an intrathoracic ramus between the T1 and T2 root has been demonstrated in this study. This corroborates the study by Jit and Mukerjee (1960). Whilst the so-called nerve of Kuntz may be evident as an isolated entity, it may show connections to components of the sympathetic chain medially (to the stellate and

2nd thoracic ganglion and to the interganglionic segment) and laterally (to the T1 intercostal nerve or the lateral cutaneous nerve of the axilla). This array in distribution has prompted a categorization of these alternate neural pathways (to Types A, B and C). Type B was noted to be more prevalent (incidence of 51.4%). Whilst Type C was least prevalent, it is possibly the most interesting. The communications to the lateral nerve of the axilla have not been previously described. This communication may be of clinical significance in primary hyperhidrosis accounting, when present, for axillary hyperhidrosis. In a cohort of 55 patients with palmar hyperhidrosis, associated axillary hyperhidrosis was noted in 32 patients (58%). Following a T2 ganglionectomy 29 patients (90%) had a satisfactory (n=3, 9.3%) or excellent (n=26, 81%)outcome. The basis for the beneficial effect on axillary hyperhidrosis following sympathectomy for palmar hyperhidrosis has long been unclear; in the light of the demonstration of an alternate pathway to the lateral cutaneous nerve of the axilla (Type C), this effect may be attributed to an unappreciated anatomical factor.

5.3.2 STELLATE GANGLION BLOCK : AN ANATOMICAL RE-APPRAISAL

The anatomical basis for a sympathetic blockade of the upper limb has been an under-appreciated issue relative to the importance of the block in the management of CRPS. Universally, the anterior paratracheal approach is probably the most popular technique. Palpation of Chassiagnac's tubercle (at the level of the 6th cervical transverse process and cricoid cartilage) is pivotal; however, the site of anaesthetic injection varies according to the practice with some injecting at the level of the 6th cervical vertebra and others at the 7th cervical vertebra. The effects of injecting at these sites has been mentioned (Guntamukkala and Hardy, 1991; Hogan et al., 1992). Further studies by Malmqvist et al., (1992) have been shown that blockade at the level of the 6th cervical vertebra produced more successful sympathetic blockade to the head and neck rather than to the upper extremities. Sympathetic blockade at the level of the 7th cervical vertebra, in contrast, produces successful sympathetic blockade of the upper extremity. Conversely, it has been suggested that a sympathetic block at the level of the 2nd or 3rd thoracic vertebrae should be used to effect upper limb sympathetic blockade (Wilkinson, 1984 and 1995; Elias, 2000a,b). Notwithstanding these recommendations, this study demonstrates that when the needle is directed in an infero-medial direction towards the antero-lateral aspect of the 7th cervical vertebral body, the thoracic chain, extending from the stellate ganglion to at least the 4th thoracic ganglion, is consistently blocked. The infero-medial technique with the injectate delivered at the level of the 7th cervical vertebra directs the solution towards a posterior route, thereby ensuring a block of the stellate and the proximal sympathetic chain.

The stellate ganglia and proximal sympathetic chain are separated from the posterior osseous structures by loose areolar tissue. This facilitates the spread of the injectate when deposited near the ganglia (Raj, 1996). This also explains the spread of the injectate to adjacent structures such as the brachial plexus, resulting in a false-positive response to the block. The spread of a local anaesthetic agent to the brachial plexus produces a somatic block (rather than sympathetic block), contributing to a negative diagnostic test. Another possibility for this phenomenon is the blockade of post-ganglionic sympathetic fibers along the vertebral and subclavian arteries (and their branches) since these structures are positioned more anterior to the stellate ganglion and is in the path of the injectate. It has also been suggested that a false positive reaction may be due to the systemic absorption of the local anaesthetic (Hogan, 1992). This explains why a large volume of injectate can misdirect the purpose of the injection (Elias, 2000a,b). For this reason, it has been suggested that a small volume of injectate could localize the spread and provide additional information about the sympathetic pathway. In current practice volumes between 10-20mls are used (Elias, 2000a,b). The quantity of an inappropriate "small" volume is unknown; a 1ml solution has been suggested for diagnostic or prognostic purposes (Elias, 2000a, b). It is apparent that a large volume may confuse the outcome and prognosis of the block. However, in the context of pain relief necessary for physical therapy or rehabilitation or to improve circulation a large volume of local anaesthetic may be useful solely for therapeutic purposes.

This anatomical study has demonstrated that whilst the stellate ganglia and proximal sympathetic chain are consistently blocked, roots of the lower trunk of the brachial plexus are also blocked when 10mls injectate is delivered. The issue of a false positive

response and a negative diagnostic test may therefore require the use of discriminatory tests to evaluate the block.

To test the efficacy of the sympathetic blockade to the upper limb several methods have been used. This may be necessary since the presence of a Horner's Syndrome does not necessarily indicate a complete interruption of the sympathetic outflow to the upper extremity, a situation predisposed when the inferior cervical ganglion is separate from the T1 ganglion. Clinical examination, which includes dilatations of the veins in the upper extremity, is inconclusive. A successful sympathetic blockade shows 5 criteria viz.

i. Horner's Syndrome within 300 seconds

ii. 1° to 30°C temperature increase

iii. An increase in blood flow by 50% or more from the pre-block state

iv. Abolition of skin resistant response on the radial and ulnar side following the block

v. Increase in skin resistant response amounting to 13% or more of the pre-block value on the radial and ulnar side (Malmqvist et al., 1992)

In practical terms, the Horner's Syndrome apart, the aforementioned are rarely applied consistently to diagnose a successful block. Like other methods used to predict a complete sympathetic block (eg. pulse amplitude changes, micro-neurography and sweat testing) these tests may be difficult to quantify, require elaborate equipment and experience and may be cumbersome, time-consuming and not well accepted by patients.

Of these tests mentioned, temperature measurement is probably the most practical technique to assess completeness of the sympathectomy.

In our practice, a blind paratracheal technique is used; the failure to instill the inject ate at a consistent point (i.e at C6 vs C7 level) most probably contributes to a varied extravasations and thereby an unpredictable outcome.

The difficulty of procuring an isolated sympathetic block using a "blind' technique has prompted the use of various localizing techniques. These include use of Magnetic Resonance Imaging (MRI), Computerised Tomography (CT) scan and fluoroscopy. Often these modalities are not available. Furthermore, the effectiveness of these modalities, whilst attractive, await objective demonstration of their value. In the light of the effectiveness and safety of therapeutic sympathectomy and the problem of sympathetic blockade, the need to accurately localize sympathetic outflow in patients present with clinical features of CRPS is a moot point. Furthermore, persistent sympathetic blockade (particularly with large volumes of local anaesthetic) may provoke fibrosis along the surgically significant component of the sympathetic chain. This, as described, may render subsequent surgery hazardous; indeed thoracoscopic sympathectomy may not become possible because of the development of adhesions.

This anatomical study has demonstrated that the infero-medial injection of 10ml of Toludine Blue Solution will consistently block the stellate ganglion and the proximal sympathetic chain. The clinical applicability of this approach awaits clarification. The pitfalls of this technique aside, we suggest that this technique be reserved for therapeutic purposes particularly when sympathectomy is not contemplated.

5.4 PATHOLOGICAL CONSIDERATIONS

5.4.1 PRIMARY HYPERHIDROSIS

To date, primary hyperhidrosis has been attributed to an exaggerated physiological response. The credibility for this inference has been the inability to identify pathological alterations in either structure or function of the sweat glands. Furthermore, there are no additional pathological changes associated with this condition.

In contradiction to this, clinical observations do allude to factors other than physiologic over-expression for manifestation of the symptoms. These include:

- There is a strong familial association suggesting a genetic predisposition. This is unlikely to be X-linked as sexes are affected equally. This observation has been made by most units that have an interest in the condition (Adar, 1977; Mares, 1994).
- Surgical management of palmar hyperhidrosis, whilst it is effective and enduring, is attended by an unpredictable response with respect to sweating in other areas. It may result in resolution of the not uncommonly associated plantar and axillary hyperhidrosis or, may even result in truncal hyperhidrosis that in itself may prove disabling to the patient. This latter symptom is more predictable with the more extensive ganglionectomies (Shelley, 1960).
- Routine staining of the ganglia done to confirm surgical excision has revealed the presence of an inflammatory infiltrate. This has not been described previously.

These factors favoured the hypothesis of an autoimmune disease with the target structure being the sympathetic ganglia and the excessive sweating a manifestation of the disease in the sympathetic ganglia rather than a disorder of the sweat glands.

Substantiating this hypothesis requires the demonstration of

- Genetic susceptibility
- Immune response directed at self-antigens peculiar to the sympathetic ganglia
- Alterations in sympathetic outflow as a result of this disease process

Identification of genetic susceptibility

It is well established that autoimmune conditions occur in genetically vulnerable individuals. Various MHC (Major Histocompatibility Complex) alleles of both class I and class II origin have been identified that have been unequivocally linked with autoimmune disorders (Theofilopoulos, 1995).

While this has not been investigated in these patients, the evidence for genetic susceptibility can be inferred from the strong familial association. It is not uncommon to find a parent and offspring as well as siblings being equally debilitated by the condition. In closed communities it is fairly common to find this condition affecting members across families.

Others have noted this observation (Adar, 1977; Mares, 1994).

Immunological response

In an organ-specific autoimmune disease, the immune response is directed to a target antigen unique to that single organ or gland, so that the manifestations of the disease process are largely limited to that organ. The target organs may be subject to direct cellular damage by humoral or cell-mediated mechanisms; alternatively, the function of a target organ may be stimulated or blocked by autoantibodies.

Identifying the defect underlying human autoimmune diseases has been difficult; information has largely been gleaned by characterizing the immune defect in the various animal models. All the animal models have implicated the CD4 T cell as the primary mediator of autoimmune disease (Haskins, 1990; Liblau, 1990).

Given the difficulty in determining the target antigen, we used cell surface markers to phenotype the inflammatory cells that infiltrated the ganglia. We attempted to determine whether there were significant CD4 T cells in the inflammatory infiltrate as well as to attempt to determine whether the subsequent response was humoral or cell mediated. The presence of a significant CD4 population of T cells in the lymphocytic infiltrate supported this autoimmune hypothesis. Additional cell surface markers showed a significant infiltrate of CD8 cells as well as CD20 cells, markers for cytotoxic T cells and mature B cells respectively. Overall, the cell counts showed a much higher proportion of cytotoxic T cells rather than B cells favouring a predominantly cell mediated response (Liblau, 1995). Although acute inflammatory cell markers were identified, the counts were not found to be significant.

In addition to the above cellular elements, all ganglia that were evaluated consistently demonstrated the presence of fibrosis that was statistically significant. A well established hallmark of auto-immune disease is the replacement of the target structure with connective tissue, lending further credibility to the pathogenesis being auto-immune in origin.

Sympathetic outflow disturbances

The sympathetic outflow disturbance has been well described; sympathetic denervation of the palms results in the abolition of the disorder. This may be attended with resolution of symptoms affecting other areas such as the plantar surfaces and axillae suggesting that the diminution in the target antigens may abrogate disease. In contrast, a significant percentage of patients develop truncal hyperhidrosis. This suggests that other (or unexicised) sympathetic ganglia are affected.

A significant chronic inflammatory infiltrate comprising CD4 T cells, CD8 T cells and mature B cells in sympathetic ganglia coupled with the clinical observation of a familial tendency favours the hypothesis of an autoimmune component for the disorder of primary hyperhidrosis. The disorder manifests at various stages in childhood in keeping with an autoimmune disease precipitated by either an infection or an immune reaction to microbial products that share homology with self-antigens as has been described for Heat Shock Protein 60 in tuberculosis (Jones, 1993). The consistent presence of fibrosis in the ganglia corresponds with the connective tissue replacement prevalent in autoimmune disease.

Further investigations needed to substantiate this hypothesis would include identification of MHC alleles that predispose to the condition, cytokine markers in the CD4 cells favouring a Th1 type response and, identifying a target antigen peculiar or significantly expressed by the sympathetic ganglion.

5.4.2 CHRONIC REGIONAL PAIN SYNDROME

Interruption of the pain cycle early in the course of the disease in CRPS is crucial to affect a satisfactory outcome. Failure to do so can result in a significant morbidity that even includes limb loss.

The difficulty in providing effective therapy for CRPS stems from an inability to reconcile all of the changes that occur in the disease process with a unified pathophysiological process. Subsequently, treatment has been directed at symptomatic relief and these have been directed at terminal factors such as nerve membrane stabilizing drugs or symptomatic agents such as analgesics.

There is ample evidence of pathological changes that perpetuate the disease process. The precipitant to the response is usually trauma to peripheral nerves that may be either innocuous or overt. Perpetuation and progression of pain is invariable; to date, the reasons for this remain elusive.

Our recourse to early sympathectomy, rather than perseverance with medical therapy, has demonstrated that these patients always have a satisfactory clinical outcome. While the relationship of sympathetic innervation and its importance in the pain pathogenesis

remains controversial, a more pivotal role was hypothesized when routine histological examination to confirm the excised sympathetic ganglion also revealed an inflammatory infiltrate. This prompted the hypothesis that the peripheral injury prompted an inflammatory response that recognized self-antigens that are normally sequestered from the immune system and this resulted in the perpetuation of the pain response.

It is well recognized that self-reactive T cells can persist in the circulation especially to self-antigens that they are not exposed to during development and subsequent thymic maturation (Kronenberg, 1991). These self-reactive T cells are anergic either due to a low expression of the self-antigen or the self-antigens are sequestered from the immune system by location. They can become clonally expanded either due to exposure to cross-reacting antigens from microbes or microbial products (Jones, 1993) or, consequent to trauma, these normally protected self-antigens are exposed to these immuno-competent cells stimulating a response. Additionally, trauma would induce changes that may see the expression of or increase in MHC expression making them vulnerable to the immune system (Feldmann, 1993).

Against this background, an autoimmune hypothesis is proposed to explain the pathophysiological changes that occur in CRPS.

Exposure of self-antigens

Neural tissue and their products are largely sequestered from the immune system and self-antigens are not normally present on the surface. Trauma results in the disruption of these structures making these antigens available for expression by antigen presenting cells. Additionally, stimulation of the local tissues by the inflammatory response can

result in the upregulation of both class I and class II MHC molecules, an effect mediated by IFN γ, on the injured tissues rendering them more susceptible to injury as a response by the immune system.

Credibility for this would be that CRPS is always preceded by trauma to the peripheral nerves and less commonly by nerve infections such as Herpes Zoster. This renders the possibility of self-antigens to become exposed from the nerve fibres. A second possibility is that this stimulates the neural cells in the ganglion to upregulate the receptors and hence the localization of the response to the affected sympathetic ganglia.

Of note, this effect occurs in selective patients. Whether this is due to genetic susceptibility remains unclear as the nature of the triggering event is unlikely to provide a sample population to substantiate this.

Demonstration of progressive inflammation

Cells in the sympathetic ganglia demonstrate a significant infiltrate of CD4 and CD8 positive cells. The high percentage of CD8 cells favours a Th1 type response being mediated by the CD4 cells present (Haskins, 1990; Liblau, 1995). This is widely accepted as the dis-equilibrium favouring the progression of an autoimmune process. There are also significant levels of mature B cells as evidenced by CD20 staining and macrophages as demonstrated by the staining for the CD68 marker. This lends credibility to the hypothesis of sequestered self-antigen exposure as well as up-regulation in the ganglion cells of MHC molecules (Theofilopoulos, 1995). This is currently being investigated.

In addition to these findings, fibrosis is invariable in these ganglia. It is well recognized that autoimmune diseases that are organ specific results in a progressive connective tissue replacement of the targeted tissue. These changes must be viewed in the light that these ganglia are remote from the primary traumatic insult.

The focal nature of the ganglion involvement would suggest that the original injury triggers the expression of MHC alleles not normally expressed by these cells circumventing a global sympathetic ganglia involvement.

Altered function and therapeutic effects

Functional impairment attests to the original insult but the accompanying aberrant sympathetic activity accompanying the injury cannot be explained by the primary insult. These changes are usually progressive and the significance of the sympathetic system has been long documented given the historical terms for the disease such as Reflex Sympathetic Dystrophy. Additionally, sympathetic blockade is not enduring and ranges from no effect to an effect that lasts longer that the duration of the anaesthetic agent used. This would favour that the sympathetic component perpetuates the disease process and this is consolidated by the predictable response from the performance of early sympathectomy in these patients.

These effects would also explain the alterations in the dorsal root ganglia as cytokines are known to cross into the central nervous system and would influence the alterations such as increased sprouting that has been reported to occur in the dorsal root ganglia in CRPS.

The sympathetic mediated effects accompanying CRPS are most likely due to the inflammation of the sympathetic ganglia. This may play a pivotal role in the disease process that results in perpetuation and progression of the disease. An autoimmune mechanism as result of sympathetic nerve disruption is an attractive hypothesis given the inflammatory infiltrate recognized in these ganglia. The fibrosis lends credibility to this hypothesis. Furthermore, that this does not occur in all patients suggest genetic vulnerability supporting our hypothesis.

Further investigations that would support this hypothesis would be the demonstration of the upregulation or expression of MHC molecules on ganglion nerve cells.

CHAPTER 6

CONCLUSION

6.1 CLINICAL CONSIDERATIONS

The primacy of thoracoscopic sympathectomy (with respect to safety, cost, and ease) is endorsed in this study, establishing this technique as arguably the brightest strand in the tapestry of minimal access surgery.

The commonest indication for upper limb sympathectomy is palmar hyperhidrosis; presently, the heightened public awareness of the safe and effective treatment for palmar hyperhidrosis has led to ever increasing numbers of this procedure being undertaken (Appendix 5).

A limited 2nd thoracic ganglionectomy is always successful for palmar hyperhidrosis; associated axillary and plantar hyperhidrosis may also be successfully treated in up to 81% and 53% respectively by limited ganglionectomy.

In patients with CRPS sympathectomy is effective when undertaken within 3 months of onset of symptoms. There is a poor outcome when sympathectomy is undertaken belatedly. The stellate ganglion block was noted to be non-predictive in defining patients who would benefit from sympathectomy.

With respect to anaesthetic technique, a single-lumen endo-tracheal tube was noted to be safe, effective and associated with less post-operative discomfort when compared to the double-lumen endo-bronchial tube.

6.2 ANATOMICAL CONSIDERATIONS

Alternate neural pathways (ANP) to the upper limb were noted in 90% of cadaveric dissections; 3 types of ANP were defined. The commonest variation was Type A, noted in 46.3%. Type B, the original nerve of Kuntz, was noted in 26.8 %. Type C was noted in 17.1 %.

When correlated to clinical outcome to an isolated 2nd ganglionectomy these ANPs are not considered to be of surgical significance.

When a modified anterior approach to the stellate ganglion block is undertaken, the clinically significant 2nd thoracic ganglion is consistently blocked. This may have clinical significance, notwithstanding the often-associated blockade of the lower trunk of the brachial plexus.

6.3 PATHOLOGICAL CONSIDERATIONS

There is strong evidence for an autoimmune hypothesis in both primary hyperhidrosis as well as CRPS. The mechanisms responsible for the development of the symptoms in these conditions appear to be different.

Further investigations would be required to better define the immune mechanisms and effects.

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APPENDIX

APPENDIX 1

SYMPATHECTOMY (1992-2001): INDICATIONS

	Palmer hyperhidrosis		CRPS		Raynaud's		PVD	
Year	Patients	Operation	Patients	Operation	Patients	Operation	Patients	Operation
1992	17	34	-	-	-	-	-	-
1993	39	78	2	2	1	2	-	-
1994	42	83	3	4	1	2	-	-
1995	61	121#	2	2	-	-	-	-
1996	56	109••#	3	3	-	-	-	-
1997	59	116•#	3	3	-	-	-	-
1998	68	134•#	5	5	2	4	1	1
1999	57	113▲	8	8	1	1	-	-
2000	31	61•	9	9	-	-	1	1
2001	18	35•	7	7	-	-	1	1
	448	**884**	**42**	**43**	**5**	**9**	**3**	**3**

Key :

- • procedure abandoned (lung adhesions- failure to collapse lung)

undertaken unilaterally for persistent sympathetic activity

▲ undertaken unilaterally for recurrent sympathetic activity

SYMPATHECTOMY UNDER TAKEN 1992-2001		
	Patients	**Operation**
Palmer Hyperhidrosis	448	884
CRPS	42	43
Raynaud's	5	9
Peripheral Vascular Disease	3	3
TOTAL	**498**	**939**

Thoracoscopic sympathectomy was successfully undertaken on 884 occasions (out of a possible total of 890); in 6 cases because of lung adhesions, a pneumothorax could not be attained and a procedure was abandoned. Unsuccessful outcome to sympathectomy (in the 890 procedures) was as follows:

i) at 3 months 2 had pSA; i.e. 880/882 = 99.77%

ii) at 1 year 4 had pSA, 2 had rSA; i.e. 877/882 = 99.43%

CAUSES OF UNSUCCESSFUL SYMPATHECTOMY

a) Failure to attain collapse (n=6)

b) Persistent sympathectomy activity (n=4); No anatomical reason noted at re-thoracoscopy

c) Recurrent sympathectomy activity (n=2) : Regenerated sympathectic chain (n=1); Dense scarring (n=1)

APPENDIX 2 (i)

CHRONIC REGIONAL PAIN SYNDROME : GROUP I

PATIENT DEMOGRAPHICS AND OUTCOME (ON LAS) FOLLOWING SYMPATHECTOMY

NUMBER	SEX	AGE	DURATION	SGB	ROUTE	PRE-OPERATIVE	POST-OPERATIVE	DIFFERENCE
1	F	31	1.50	1	TS	10.0	4.2	5.8
2	M	30	1.00	1	TS	9.2	1.0	8.2
3	M	23	1.75	1	TS	8.6	0.5	8.1
4	M	45	1.25	1	TS	8.4	2.1	6.3
5	M	28	1.50	1	TS	9.0	1.0	8.0
6	M	26	1.00	1	TS	7.8	0.6	7.2
7	M	38	2.25	1	TS	10.0	3.8	6.2
8	M	27	1.75	1	TS	8.1	0	8.1
9	M	42	1.50	1	TS	8.9	1.9	7
10	F	26	1.50	1	TS	9.2	1.0	8.2
11	M	24	2.75	2	TS	8.9	3.0	5.9
12	F	32	2.00	1	TS	8.5	0.2	8.3
13	F	28	1.50	1	TS	9.6	0.4	9.2
14	M	33	1.50	1	TS	10.0	0	10
15	F	32	2.00	1	TS	9.4	1.0	8.4
16	F	28	2.50	1	TS	9.6	1.5	8.1
17	F	45	2.00	1	TS/OS	9.6	1.0	8.6
18	M	47	2.50	1	TS/OS	9.7	2.0	7.7
19	M	24	1.50	1	TS	9.0	1.0	8
20	M	17	2.50	1	TS	9.5	1.5	8.0
21	M	22	2.00	1	TS	9.0	1.0	8
22	M	26	2.50	1	TS	8.0	4.0	6
23	F	36	2.00	1	TS	7.5	3.5	4
24	M	26	1.70	1	TS	9.0	2.0	7

Key :

Group = symptoms evident for $< {}^{3}/_{12}$

SGB = Number of stellate ganglion blocks performed

Route = TS - Thoracoscopic sympathectomy

TS/OS - Thoracoscopic converted to open sympathectomy

OS - Open sympathectomy

Difference = Difference in outcome i.e score

APPENDIX 2 (ii)

GROUP II : GRPS

GROUP 2	SEX	AGE	DURATION	SGB	ROUTE	PRE-OPERATIVE	POST-OPERATIVE	DIFFERENCE
1	F	50	5.00	1	TS	7.0	3	4
2	M	23	4.00	3	TS	9.8	4.6	5.2
3	F	30	4.25	4	OS	8.8	3.8	5
4	M	27	8.00	4	OS	10.0	9.2	0.8
5	M	64	3.50	3	TS	9.2	0.2	9
6	M	36	4.50	3	OS	8.7	3.1	5.6
7	F	40	7.25	4	OS	9.9	8.9	1
8	M	31	3.75	3	TS	8.1	1.2	6.9
9	F	52	12.25	5	TS	9.7	7.9	2
10	F	36	5.25	2	OS	9.7	0.8	8.9
11	M	29	9.00	4	OS	10.0	9.4	0.6
12	M	32	12.00	1	TS	8.0	3	5
13	M	48	13.00	4	TS	9.6	9	0.6
14	F	47	84.00	1	TS	8.6	3	5.6
15	M	38	48.00	4	TS	8.0	6	2
16	M	50	24.00	1	OS	8.0	6	2
17	F	41	36.00	2	TS	9.0	1	8
18	F	31	19.00	1	TS	10.0	4.5	5.5
19	M	42	24.00	1	TS	7.5	1	6.5

Key :

Group = symptoms evident for $< {}^{3}/_{12}$

SGB = Number of stellate ganglion blocks performed

Route = TS - Thoracoscopic sympathectomy

TS/OS - Thoracoscopic converted to open sympathectomy

OS - Open sympathectomy

Difference = Difference in outcome i.e score

APPENDIX 3

LIMITED GANGLIONECTOMY: PRE-*vs* POST- OPERATIVE SCORING ON VLAS

PALMAR HYPERHIDROSIS (PH)			AXILLARY WITH PH			PLANTAR WITH PH		
Pre-Op	Post Op	Difference	Pre-Op	Post Op	Difference	Pre-Op	Post Op	Difference
7	1	6	9	1.9	7.1	10	1	9
8	1.2	6.8	8.8	2.6	6.2	8.6	1.5	7.1
9	1.3	7.7	9.4	3.6	5.8	9.5	1.9	7.6
10	1	9	10	2	8	7.9	2.3	5.6
7.5	2	5.5	7.8	2.8	5	9.9	2	7.9
7.9	1.2	6.7	10	2.4	7.6	9.4	2.2	7.2
8.6	1.1	7.5	8.5	2.6	5.9	8.9	3	5.9
9.3	0.9	8.4	9.5	3.7	5.8	10	2.1	7.9
9.9	0.4	9.5	9.7	2.1	7.6	9.7	1.4	8.3
10	0.6	9.4	9	1.9	7.1	9.4	1.8	7.6
9.8	0.2	9.6	9.3	1.4	7.9	8.6	0.8	7.8
9.6	0	9.6	8.5	1.3	7.2	8.9	0.9	8
8.9	0.7	8.2	8.2	1.9	6.3	9.7	2.1	7.6
10	0	10	9.6	2	7.6	7.7	2.6	5.1
10	0.4	9.6	9.3	1.6	7.7	9.8	2.6	7.2
9.9	0.2	9.7	7.3	2.9	4.4	9.2	2.1	7.1
8.9	1	7.9	7.5	1.3	6.2	8.9	0.1	8.8
9.6	0.6	9	8.6	2.4	6.2	7.9	1.1	6.8
9.5	0.9	8.6	4.7	3.7	1	8.7	0.5	8.2
9.4	0.7	8.7	5.5	2.6	2.9	10	0	10
10	1	9	6	2	4	9.9	2	7.9
8.9	2	6.9	6.8	2.2	4.6	7.9	0	7.9
7.8	0.9	6.9	6.4	1.7	4.7	9.5	0.4	9.1
9	0.3	8.7	4.9	1.8	3.1	8.7	0.1	8.6
9.7	0.5	9.2	4.6	0.9	3.7	3.3	2	1.3
10	0.2	9.8	5.6	1	4.6	9.2	2.1	7.1
9.6	0.3	9.3	6.7	5.6	1.1	8.5	4	4.5
9.5	0.6	8.9	4.8	5	-0.2	6.5	3.1	3.4
9.3	0.8	8.5	5.9	6.3	-0.4	6.3	5.4	0.9
9.2	0.7	8.5	5.8	8.1	-2.3	5.4	4.6	0.8
9.1	0.9	8.2	2.3	9.8	-7.5	5.7	5.7	0
9.6	0.2	9.4	2.4	9.5	-7.1	5.4	4.2	1.2
9.9	0.3	9.6				6.3	3.2	3.1
9.7	0	9.7				5.3	4.3	1
9.3	0.4	8.9				5.8	4.8	1
9.5	0.1	9.4				6.8	3.6	3.2
9.2	0.4	8.8				5.7	4.1	1.6
9.5	0.2	9.3				5.9	5	0.9
9.8	0.5	9.3				6.7	7.6	-0.9
9	0.5	8.5				5.8	4.7	1.1
9.1	0.3	8.8				5.9	4.3	1.6
9.3	0.1	9.2				6.3	4	2.3
9.6	0	9.6				6.9	4.2	2.7
9.6	0	9.6				2.5	4	-1.5
9.8	0	9.8				2.9	5	-2.1
10	0.7	9.3				2.5	5	-2.5
10	0.3	9.7				3.9	6.5	-2.6
8.9	0.1	8.8				3.8	7.3	-3.5
7.9	0.2	7.7				2.9	8	-5.1
9	0.1	8.9						
9.6	0.1	9.5						
9.7	0.4	9.3						
9.2	0.2	9						
9.4	0.6	8.8						
9.8	0.9	8.9						

APPENDIX 4

NERVE OF KUNTZ : DISTANCE (mm) FROM SYMPATHETIC INTERGANGLIONIC SEGMENT (BETWEEN STELLATE AND T2 GANGLIA)

TYPE A (n=17)		TYPE B (n=11)		TYPE C (n=7)	
Right (n=8)	*Left (n=11)*	*Right (n=4)*	*Left (n=7)*	*Right (n=3)*	*Left (n=4)*
2.7	4.6	6.0	12.3	8.0	12.0
3.0	5.0	15.3	6.0	1.0	9.0
2.4	8.0	4.0	10.0	9.0	4.5
8.7	10.5	4.5	9.0		11.0
6.0	7.5		7.0		
30.0	2.5		5.0		
3.7	3.5		4.8		
9.0	8.0				
	6.0				
	5.4				
	7.5				