

From Mitchell's causalgia to complex regional pain syndromes: 150 years of definitions and theories

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It is not unusual in rheumatological or rehabilitation settings to encounter patients with a combination of pain, trophic disorders of the skin and adnexae, vasomotor alterations and sweating, who are typically classified as having algodystrophy or an even more generic, although regionally localised, complex pain syndrome (CRPS). Our limited understanding of the pathophysiology of this condition is not only reflected by its generic classification, but also in the myriad of pharmacological, instrumental, rehabilitative, and alternative treatments tried by various groups with little success. The use of the systemic administration or loco-regional injection of drugs, all forms of electrotherapy, hot and cold thermal treatments, LASER therapies, every type of kinesiotherapy, and a long series of unconventional treatments all go to show that it is impossible to establish an effective treatment of any kind in the absence of clear physiopathological information. This article will not deal with the various treatments described in the literature (even though they merit further consideration), but will summarise what is currently known about the pathophysiology of algodystrophies as an indirect means of laying the basis for their rational treatment. In the case of these diseases, new theories do not always replace their predecessors but, in many cases, both continue to survive together and so we will outline the history of the scientific ideas that have led to the recognition of the reflex sympathetic dystrophies (Table 1) that are currently taxonomically categorised complex regional pain syndromes (1) in the hope that this will make the information more complete and palatable.

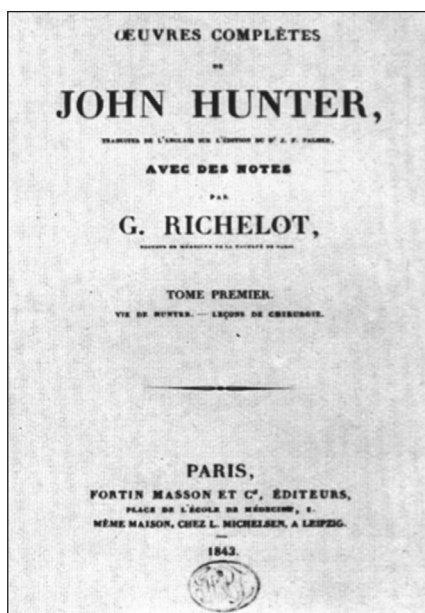
First of all, in an attempt to free ourselves of the taxonomic confusion that reigns in referral requests for treatment

(and not only in the rehabilitation setting), it is worth considering the truly striking number of terms that have long been used to describe what are essentially the same events that are now seen as the final clinical picture of a number of sometimes poorly understood mechanisms. When running through these definitions, what is immediately noticeable is that researchers switched their attention away from their initial aetiological emphasis on traumatic inflammation and towards the cognitive/behavioural aspects of the condition, the recognition of a reflex action that occurs both locally and in the spinal cord, vegetative vasomotor effects and possible constitutional/genetic co-causes by formulating the neurovegetative hypothesis of a *vicious circle*, and have now developed the current neuroreceptor hypothesis as an ideal means of closing a virtuous circle that takes us back to where we started in the periphery. However, despite this remarkable progression and the undoubted therapeutic advantages it generated, there is still (and will probably remain for some time) a lack of any precise knowledge of the exact mechanisms by means of which the nervous system:

- i) fails to recognise sensorial afferents and therefore makes incongruous responses;
- ii) becomes itself a producer of a continuous state of pain under the constant of afferent barrages;
- iii) reacts by increasing its own excitability in an attempt to fill the silence caused by sensory deprivation.

Fortunately, almost all researchers have now abandoned the idea that there is a preferential route for pain within the nervous system, and concentrate on the plasticity and control of information. The importance of the traumatic aetiology, bone and dystrophic altera-

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tions, the vascular system, the sympathetic drive, cognitive-behavioural components, and peripheral receptors is not due to place in new models of understanding pain, but to their individual roles as players of one great (and unfortunately cacophonous!) symphony. Not even the new discoveries capable of opening up very important therapeutic strategies for what is now called intractable pain will ever lead to a single magic *painkilling pill* because the mechanisms that allow nerves to maintain the stability of their own activity (even when this is tragically out of tune) are too numerous and too interconnected.

John Hunter (1766) was probably one of the first scientists of the modern era to draw the attention of clinicians to the traumatic aetiology of the pain syndromes associated with muscle and joint atrophy (2). However, it was not until the American War of Independence (1861–1865) that Weir Mitchell, Morehouse and Keen (1864) carefully observed and described the aspects of some pain syndromes that recall those indicated by Hunter.

The American Civil War was responsible for an enormous number of fire-arm wounds leading to amputations and various forms of neuritis due to the presence of bullets and shot near neurovascular bundles and incomplete nerve lesions. Upon the orders of the Surgeon General of the American army, Dr W.A.

Table I. A history of the scientific ideas that have led to the recognition of the reflex sympathetic dystrophies.

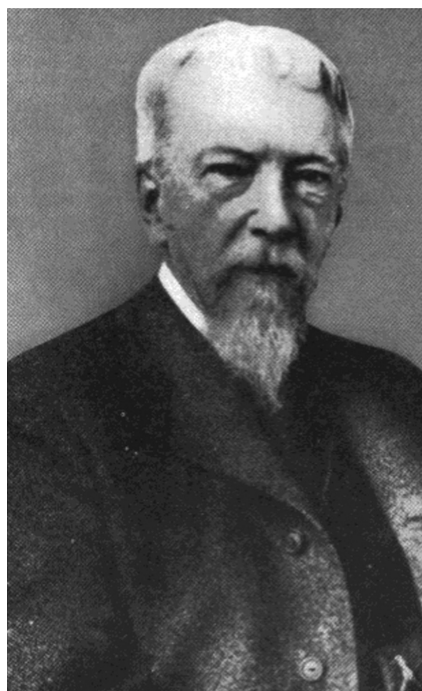
Causalgia	Weir Mitchell	1864
Trophoneurosis	Wolff	1877
Acute bone atrophy	Sudeck	1900
Post-traumatic painful osteoporosis	Leriche	1923
Acute peripheral neuroatrophy	Zur Vert	1923
Traumatic angiospasm	Morton & Scott	1931
Post-traumatic osteoporosis	Fontane	1933
Traumatic vasospasm	Lehman	1934
Reflex limb dystrophy	De Takats	1937
Minor & major causalgia	Homans	1940
Post-infarction sclerodactyly	Johnson	1943
Shoulder-hand syndrome	Steinbrocker	1947
Reflex sympathetic dystrophy	Evans	1947
Algodystrophy	De Seze	1954
Osteodystrophy	Lenggenhager	1971
Causalgia minor	Patman	1973
Algo-neuro-dystrophy	Glick	1973
Sympathetic sustained pain syndromes	Roberts	1986
Sympathetic dependent pain	Churcher & Ingall	1987
Hyperactive sympathetic syndrome	Hannington-Kiff	1989
Reflex sympathetic dystrophies (RSD)	Bonica adopted by Evans	1990
Complex regional pain syndromes (CRPS)	IASP	1994
Complex regional pain disease (CRPD)	Niv	2004

Hammond, all of the patients with traumatic lesions of the nervous system were taken to the 400-bed Turner's Lane Hospital in Philadelphia where Mitchell operated and observed that, although many of the wounds healed, they left pain persisting for months and, frequently, for years. It is interesting to note that, even at that time, the treatment of neuritis and causalgias fa-

voured by Mitchell was *local* injections of morphine combined with physical treatments such as the application of damp compresses. The dramatic nature and importance of the phenomena observed by Mitchell were demonstrated by the fact that, in one year, the incredible number of 40,000 morphine used in the treatment of pain (3).

Mitchell's work is considered pivotal not only because of the number, but also because of the quality of his observations. What follows is his differential description of the sensory disorders caused by neuritis and neuralgia, and those due to causalgia (a term coined by Mitchell himself, drawing on the *Collectio Hippocratica*, which has become a cornerstone in the history of pain medicine.

"Subacute neuritis is difficult to diagnose when it is of average intensity and does not result from a traumatic accident... The affected nerve is sensitive for a considerable part of its trajectory, the points of emergence from the bones or aponeuroses are the most painful. By contrast, in genuine neuralgia, the Valleix's points are the only ones which produce acute pain in response to pressure. Contrary to neuralgic hyperaesthesia, that of neuritis is uniform and constant at all times".



Silas Weir Mitchell

"In our clinical practice we have frequently encountered patients who complained of very acute pains, which they themselves compared to a burn, or to the action of a very hot mustard plaster, or to the effect of a red-hot file abrading their skin" (Mitchell, 1874) (4).

Throughout Mitchell's reports, it is clearly apparent that he considered causalgic pain and the connected vasomotor and atrophic disturbances as the result of the accumulation and mutual reinforcement of various factors capable of maintaining pain in a vicious circle. In his writing of 1874, he is clearly critical of the then dominant idea of a specific pain transmission system, and his concept of a vicious circle proved to be a great scientific success even before it was fully taken up by Livingston in 1947.

Although his name is not specifically linked to the algodystrophies, it is nevertheless worth noting the extraordinary foresightedness of the ideas expressed by Charcot in his description of a case of post-traumatic atrophy observed at Salpêtrière hospital. He emphasised that there was no relationship between the intensity of the stimulus and the severity of the atrophic and paralytic picture, and that the only plausible explanation was that of spinal hyperexcitability, which he called spinal deuteropathic disorder (Charcot, 1883). Unfortunately, although this concept of a variable link between stimulus and pain intensity was repeated continuously by Wall, it has still not been fully absorbed by all of us who are actively involved in the treatment of pain, and we still tend to consider only the clinical situations for which we can physically identify an anatomical lesion as very painful.

Vulpian's theory of reflex atrophy (1886) was the first to suggest that the irritable state induced by a pathological process causes a reflex mechanism (5). Following on the coat-tails of Sherrington's physiology, he considered that atrophic disorders were due to reflex spinal activity generating trophic alterations – a hypothesis that was indirectly supported by a brilliant experiment in which it was observed that when the dorsal roots were transected on one

side, joint inflammation only occurred in the normally innervated limb.

During the same period, in parallel with such Sherringtonian-based theories, other authors (including Strumpell, Charcot and, later, Wolff) were developing a line of research in which they interpreted algodystrophies as disorders with a predominantly hysterical component for which Wolff (1877) coined the term trophoneurosis (6, 7).

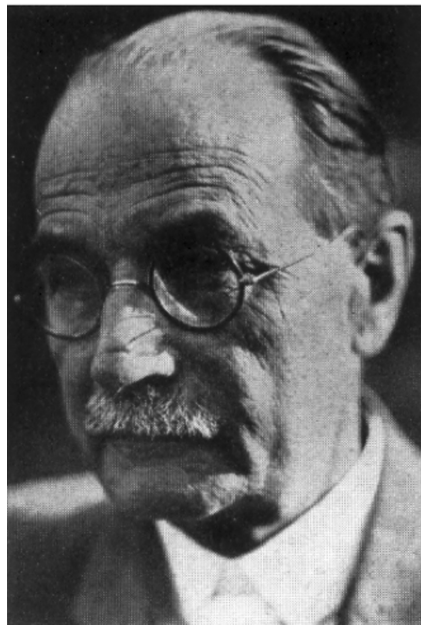
In 1898, the French journal *Echo Médicale de Lyon* published an article by Destot and Morusset that opened the way to the work of Sudeck (8, 9). The article described the radiological picture of osteoporosis in a patient affected by intractable pain resistant to every type of therapy, which had started after a trauma to the ankle. The authors interpreted this radiological picture of maculated bone atrophy as senile osteoporosis. However, the difference between the pictures of senile osteoporosis and the osteoporosis seen in patients with reflex sympathetic algodystrophy did not escape Sudeck. Two years later, at the 29th Congress of the German Society of Surgery, he presented a study in which the radiological features of chronic bone atrophy – senile osteoporosis – were clearly differentiated from those of acute post-traumatic osteoporosis (Sudeck, 1900). This distinction was to lead to his name being insepara-

rably associated with a new nosological entity: Sudeck's post-traumatic atrophy, Sudeck's atrophy, Sudeck's post-traumatic syndrome or, in some texts, simply Sudeck.

Sudeck published works concerning post-traumatic osteoporosis until the 1940s, modifying and refining his etio-pathological view from an initially predominantly peripheral, inflammatory concept in which the symptoms were interpreted as an expression of local hormonal or biochemical phenomena (Sudeck, 1900) to full recognition of a reflex action of the nervous system (Sudeck, 1938). However, given his training as an orthopedic surgeon, Sudeck never tackled the problem of the nerve pathways involved but, like his contemporary, Bier, placed great emphasis on peripheral aspects and the involvement of periarticular soft tissues as expressions of the same pathological process he called "collateral inflammation".

He used his last research period between 1938–1943 to summarise and organise his thoughts, and identified some of the aetiologies capable of causing algodystrophy: i) trophic limb disorders secondary to peripheral irritation of any kind; ii) post-thrombophlebitic forms with lymphatic alterations; and iii) neurotrophic disorders following poliomyelitis, herpes zoster, neuritis or peripheral nerve lesions.

In these decisive years, and undoubtedly partially influenced by the philosophical approach centred on the Greek motto *παντα ρει*, Sudeck proposed the classical division of the algodystrophies into three stages. The first (called "useful inflammation" or *Heilentzündung*) was characterised by increased metabolism and cell hyperactivity aimed at repair and restituito ad integrum, and clinically expressed by the classical signs of inflammation extending to surrounding tissues in accordance with the author's concept of collateral inflammation. This physiological stage ends when the inflammatory state or the mechanical irritation lasts longer than the time the involved tissues can support the biological commitment of reparative hyperactivity, and is followed by the second, pathological stage, which is characterised by weakening tissue reac-



Paul Sudeck

tivity, degeneration and vascular atony and has a dystrophic evolution: *i.e.* the *dystrophies*. According to Sudeck, this stage can still be directed towards healing (πάντα ρεῖ), but more often degenerates into the third stage of true atrophic sequelae: *i.e.* the *atrophies*.

It is interesting to note that, although this three stage division is still used clinically (and even forms part of the 1990 clinical classification proposed by Bonica, which we will discuss later), we have lost the concept of Heilentzündung (*i.e.* all of the events involving vasomotor sympathetic activity that are simply physiological reactions to a trauma and not yet pathological), although these reactions are some of the clinical signs normally accompanying the removal of a leg plaster cast.

A name inseparably associated with pain therapy is that of Renè Leriche, who published *La chirurgie de la douleur* in 1949, at the end of a period of research that started in 1913 when, after a stay in America, he carried out the first anterior sympathectomy. This innovative approach was developed on the basis of Claude Bernard's research into the function and integration of the autonomic nervous system, which had highlighted the vasodilatory effect that can be obtained by sectioning the sympathetic cervical ganglion. Leriche became convinced that the dystrophy, osteoporosis and pain depended

on vascular dysregulation secondary to a traumatic event, and thus suggested using the term "post-traumatic painful osteoporosis" instead of the "atrophy" championed by Sudeck. Leriche's technique was considered a fascinating potential alternative to the analgesic use of morphine, which was beginning to raise concerns within the medical profession as the cause of the increasing number of iatrogenic drug addicts. Leriche's contribution to the reflex sympathetic theory of pain was certainly not original, but he did have the merit of drawing attention to the mechanism by repeatedly emphasising the importance of axonal reflexes.

Leriche's surgical proposal is well worth careful re-evaluation (10). He considered that the success sometimes achieved with sympathetic surgery was not just related to the merely technical act of dividing the nerve pathways, but could be placed in the very stimulating context of *physiological surgery* insofar as he believed that the surgical interruption of sympathetic pathways was actually a means of affecting highly complex physiological systems.

Leriche, who was certainly influenced by the work and ideas of Claude Bernard, thought that the association of efferent motor fibres with some afferent fibres within the sympathetic nerves indicated a relationship with sensation, and believed that the sympathetic system played a role in the genesis of pain maintenance by means of three mechanisms: sensory transmission by nociceptive afferents, the vasoconstrictive efferent activity generating the pain itself, and the metabolic changes underlying the altered sensitivity to nociceptive stimuli (a surprisingly early forerunner of the current neuroreceptor hypothesis). These ideas, particularly those linked to the presence of sensory afferents within the sympathetic system, were directly challenged by the Anglo-Saxon school of thought led by Langley, who considered that the sympathetic system consisted of purely efferent motor fibres, and a similar argument can be found in Alberto Malliani's chapter in the second edition of the Textbook of Pain by Wall and Melzack (Malliani *et al.* 1989) (11).

Just as the concept of reflex sympathetic activity is associated with the name of Leriche, the concept of the vicious circle (which had already had a certain scientific success) is now associated with that of Livingston (12), who took it up in 1947, and made it a working paradigm that is still apparently dear to many pain therapists. It may be useful (if not fundamental) but, like the other great theory of pain known as the gate hypothesis, is certainly inadequate even though it is still used in various forms by authoritative contemporary researchers such as Blumberg, Bennet, Boas, Janig and Stanton-Hicks.



William Kenneth Livingston

Livingston considered as something very different: instead of being a simple reaction, he saw it as a subjective sensory experience that often exceeds its property of acting as an alarm signal, becoming destructive under the influence of afferent barrages, and making the nervous system itself the generator of continuous pain. In the preface to his 1947 monograph "Pain Mechanisms. A Physiologic Interpretation of Causalgia and its Related States", Livingston openly related his work to that of Mitchell by saying:

"...he shows that a partial lesion of a nerve may be more capable of mischief than complete division, and expresses his conviction that the mischief is, to a large degree, the result of a vicious circle of spreading reflexes, having as their source an irritation of sensory nerve filaments. When the later pathological changes of an irritative nature which follow nerve injuries begin to



Renè Leriche

occur, new causes of pain arise, the reflex become wider, and when in certain cases nutrition of the skin suffers, novel forms of suffering spring up which are due to alterations of the peripheral nerve ends or their protective tissues. These views expressed so many years ago come very close to stating the central theme of this monograph, so much so that I regard my investigation as an attempt to carry forward the original work of Weir Mitchell".

The monograph not only deals with the problem of algodystrophies, but roams through all of the sectors of pain together their psychological and physiological features. His interest in the psychological aspect of pain bears witness to his open criticisms of the concept of the specificity of the transmission of pain impulses, but also to Livingston's commitment against pain as suffering, as is further demonstrated by the title of the never published book (*Pain and Suffering*) he was writing when he died of a heart attack in 1966.

We will here mention just two of Livingston's many splendid observations. The first is his suggestion of using a diagnostic block of the sympathetic system with local anesthesia before ganglionectomy as an indicator of the value of the final result (... *some index of the value of sympathectomy*...). The second is his description of the effect that blocking blood circulation has on hyperesthesia, which anticipates all of the contemporary studies of the role of A-beta fibres in the genesis of some types of pain.

J.J. Bonica was not only an extraordinary scientist and researcher, but also a man of incredible humanity we are pleased to be able to remember here (13, 14). Born on the island of Filicudi in Sicily, he emigrated to America with his family when he was ten years old and, after becoming a professional wrestler in order to support his studies, he graduated in Medicine in 1942. Shortly after receiving his degree, he was named Director of the Department of Anesthesia of Madigan Military Hospital in Washington State where, like other great men such as Mitchell and Livingston, he saw the terrible suffering caused by war as he treated service-



Wrestling World Champion
Johnny "Bull" Walker alias JJ. Bonica

men who had been wounded at Pearl Harbour, Guadalcanal and Okinawa using the technique of nerve blockade. At the end of the Second World War, by which time he had become Director of the Anaesthetic Department of Tacoma General Hospital, he summarised his experiences of analgesic blockade in a book entitled *The Management of Pain*, which was published in Italian in 1959 (the second and greatly extended edition of the book was published in 1990, with Loeser, Chapman and Fordyce as co-authors).

On the basis of his own ideas and organisational model, Bonica created a school of thought on the coast of the Pacific Ocean that dominated the physiopathology and therapy of pain in the second half of the last century. Bonica obviously applied nerve blocks to the vegetative nervous system before ap-



J.J. Bonica (1972)

plying them to reflex sympathetic dystrophies and causalgia, and a chapter of more than 60 pages was dedicated to this subject in the book's second edition, which also introduced for the first time a chapter with the suggestive title of Regional Pain Syndromes, thus anticipating the more recent taxonomic classification of Complex Regional Syndromes proposed by the IASP in 1994.

In the chapter concerning causalgia and other reflex sympathetic dystrophies, Bonica proposed dividing them into major and minor reflex dystrophies. In both cases, and regardless of aetiology, he saw the reflex disorder arising from the sympathetic nervous system as the unifying factor, and this interpretation still greatly influences research into the physiopathology of pain.

Bonica, who reworked a classification proposed by De Takats in 1943, distinguished three stages in the evolution of the reflex dystrophies and, given its continuing clinical importance, we reproduce what was written in the first Italian edition of 1959 (15).

"The first stage is characterized by a constant, irritating, moderate pain localized to the parts affected. Hyperaesthesia, muscle spasms and pain develop and can lead to considerable limitation of movement. The skin is normally dry, pink and warm, with rare signs of vasoconstriction. In average cases this first stage lasts for some weeks, responding fairly well to appropriate therapy. In rarer cases, the first stage can last for as long as six months.

The second stage is characterized by a gradual decrease in the pain, increased oedema and increased joint stiffness. The skin is damp, cyanotic, cold and becomes less hairy. The nails appear jagged. The signs of atrophy become more evident and radiological examination shows marked osteoporosis. The pathological process in this stage can protract for as long as 3 to 6 months but is still susceptible to regression if treated appropriately.

The third stage is characterized by notable trophic lesions, which often become irreversible. The skin has become smooth, skin folds have disappeared, and the skin is pearl-coloured at low

temperatures. The subcutaneous tissue has become atrophic, as have the muscles, particularly the interosseous muscles. The limbs become extremely weak, with limitation of movements, and consequent ankylosis of the joints of the hands and feet. Osteoporosis appears to be widespread and the oscilometric traces are reduced. The pain can be moderate or intense, almost always of a dragging sort, and worsened by exposure to cold. Many patients in this third stage of the syndrome have profound mental changes as a consequence of the pain and prolonged immobility."

A first comment on Bonica's view of the aetiology of algodystrophies is that it is not far removed from the traditional view of the sympathetic hyperactivity capable of generating and maintaining the vicious 'pain-sympathetic hyperactivity-pain' circle. Bonica re-used the definition of reflex sympathetic dystrophy (coined by Evans in 1946) (16) to highlight what he considered to be the fundamental that a sympathetic blockade can interrupt the pain. This was also the direction taken by Roberts (1986) (17) who introduced the term "sympathetically maintained pain", Churcher & Ingall (1987) (18) with their "sympathetically dependent pain", and Hannington-Kiff (1989) (19), who first used Bier's guanethidine blockade and suggested the term "sympathetic hyperactivity syndrome": setting aside the protean nature of their new definitions, it is clear that all of these researchers agreed on considering increased sympathetic activity as the central part of the pathology.

A second (and already briefly mentioned) point concerns the disappearance of the concept of useful inflammation (*Heilentzundung*) favoured by Sudeck because, although Bonica's description of the three stages is clinically point and remains a landmark, it was this conceptual change that led to early medicalisation and the serious risk of generating an iatrogenic evolution towards the second stage. The fact this danger is not merely theoretical is shown by the variably invasive interventions that were until recently even proposed for first-stage algodys-

trophies: "... more recently ... there is growing certainty that the best therapeutic method, apart from surgical ablation of the causal factor, is sympathetic blockade, whether obtained by anaesthetic infiltration or surgical lysis" (Bonica, 1959).

By the beginning of the 1990s, everyone who was even only slightly familiar with the scientific literature agreed that the time had come for a detailed review, which was not only necessary taxonomically, but would also provide a sort of ideal starting point for new hypotheses concerning pain and the reflex sympathetic dystrophies that were free of the restrictions imposed by the usual theories of reflex activity and its vicious circle. Consequently, under the aegis of the IASP, a group of researchers (R. Baron, H. Blumberg, R.A. Boas, J.N. Campbell, J.D. Haddox, S.J. Hassenbusch, M. Kolzemburg, H. Merskey, P.P. Raj, M. Stanton-Hicks, and R.T. Wilder) met in 1993 in Orlando, Florida, with the precise aim of reconsidering the signs, symptoms and differential diagnosis of reflex sympathetic dystrophies in a bid to reorganise their clinical aspects and taxonomy. Their ideas, together with some other original contributions, were subsequently collected in a volume edited by Janig and Stanton-Hicks for the IASP Press in 1996 (20).

The first result of this meeting was the recognition that the term reflex sympathetic dystrophy was no longer clinically useful because it had become a sort of indiscriminate catch-all means of describing patients with signs of neuropathic pain or, even worse, all cases resistant to the therapies proposed from time to time on the basis of the supposedly pivotal involvement of the nervous system.

The second (and in our opinion, more important) result was that, for the first time, it was clearly stated that although the hypothesis of a vicious circle proposed by Livingston and supported by Bonica still retained a certain conceptual validity from many points of view, the model was no longer sufficient to explain recently published data and the conflicting results of the proposed treatments.

The third last result was the proposal of the new term "complex regional pain syndromes" (CRPS), which absorbed the old "reflex sympathetic dystrophies" (CRPS-type I), causalgia (CRPS-type II) and, described in a separate chapter, "sympathetically maintained pain" (CRPS-type III), with the last being subdivided into a further subtype that was ambiguously called "sympathetically independent pain" (SIP), which was intended to include all of the type III syndromes that do not respond to a sympathetic blockade.

Although far from perfect, this classification did at least try to eliminate a series of ambiguities such as those connecting taxonomy and the hypothesised underlying mechanism. However, despite the good intentions, the ambiguity firmly thrown out of the front door crept back in through the window because, biding dividing the CRPS into three broad types, it re-introduced the distinction of pain sustained by or independent of the sympathetic system. Furthermore, it is mentioned that sympathetically maintained pain can be associated with a variety of pathological conditions not necessarily included among the CRPS and, similarly, that CRPS can be associated with pain which more or less dependent on the sympathetic system (21).

The current distinction of CRPS with or without an apparent lesions originates as usual from the classical works of past researchers. Bonica had already tried to use the term "regional pain syndromes", and Sudeck described and distinguished trophic limb disorders secondary to peripheral irritation of any nature, including post-thrombophlebitic forms and those with lymphatic alterations, be they neurotrophic disturbances secondary to poliomyelitis, herpes zoster or neuritis, or peripheral nerve lesions in general when the lesion was obvious and clearly recognisable. In the new classification, former group are considered type I complex regional syndromes, and while the latter is exactly what contemporary authors such as Janig and Stanton-Hicks call type II complex regional syndromes: *i.e.* syndromes with a nerve lesion.

It is not yet possible to make a working

judgement concerning this proposed taxonomy because too little time has passed and the data relating to its clinical and research use are still insufficient to draw objective conclusions; all that it can be done is to describing some of its obvious contradictions. However, this classification is very important for the evolution of research because it clearly focuses on the need to understand why some types of pain are susceptible to control by blocking part or all of the sympathetic system whereas, despite their clinically similar symptoms, others are not.

Furthermore, the problem of evaluating the analgesic effects of sympatholytics has made it difficult to demonstrate their existence. Leriche considered the efficacy of sympathetic blockade an irrefutable demonstration of the involvement of the sympathetic system in the genesis/maintenance of pain, but has recently been challenged, and we must remember the possibility of false negative and positive findings, the lack of validated tests, and the technical problems associated with producing the blockade (target structure, systemic effects, etc.). Baron's observation (1999) of the presence of allodynia to cold in patients with algodystrophy is also very interesting: it is possible that Bier's technique involving sympatholytic drugs capable of producing vasodilatation (thus increasing skin temperature and decreasing spontaneous allodynia) may improve spontaneous symptoms without acting on the relationship between the sympathetic system and pain. Our lack of basic knowledge is immediately reflected in the results that can be achieved by means of physiotherapy: if it is true that the sympathetic system can sometimes maintain pain, any physical treatment that activates the sympathetic system may even increase it, not only all of the techniques involving electrical currents such as transcutaneous nerve stimulation (TENS), but also massage. A variety of now consolidated data have been accumulated showing that, regardless of its therapeutic effect, any sufficiently new stimulus first stimulates an adap-

tive sympathetic response, which, in the final analysis, means maintaining sympathetically mediated pain.

We shall not try to draw any conclusions to close this short and inevitably incomplete gallop through 150 years of definitions and theories, which has taken us from Mitchell's causalgia to the complex regional pain disease proposed by David Niv. However, we would like to recommend the introduction to the third edition of the Text Book of Pain by Patrick Wall (22), which is entitled Introduction to the edition after this because offers researchers some extraordinarily interesting ideas that go beyond the tramlines of the usual schemas and definitions.



Patrick Wall

It is also worth remembering that anyone who carries out rehabilitation research without bearing in mind that every nervous event (including pain) is the outcome of plasticity and controls in time and space within the nervous system may perhaps be able produce further brilliant papers and come up with new definitions to add to the long list described at the beginning of this article, but will never truly advance the knowledge needed to make the changes in medical practice necessary to alleviate the suffering of our patients.

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