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# Recent advances on acute paraplegia

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ABSTRACT

Paraplegia and spinal cord injuries are issues of major concern to the actual medicine. But recent advances have raised hopes for a better prognosis, which has always been poor or infaust since medicine was practiced. However and interestingly enough, some concepts and definitions on the occurrence have survived for millennia. Once encountered as an issue, traumatic or non-traumatic paraplegia needs a multidisciplinary approach and a careful staging of the problem. Different scales are available with Frankel's and American Spinal Injury Association most widely used as alternatives or complementary tools. The authors discuss therapeutic options with a special focus on the stem cell therapy which has seen an impressive increase on the number of trials for a successful treatment. Sourcing and yielding of stem cells are made possible through a number of techniques, with material aspirated from bone marrow or adipose tissue, which are used along with other sources of neuronal precursors such as olfactory ensheathing cells. Nevertheless, large and multicenter studies are still lacking. However, with the quality of the ongoing work and research, the optimistic attitude seems warranted. Meanwhile, other rehabilitation and medical care interventions, always at hand, need to be applied in every individual suffering from paraplegia and spinal cord injury.

## 1. Introduction

The traumatic, and even more the non-traumatic paraplegia, always remaining a diagnostic and clinical challenge, has been a part of medical discussions and publications ever since quotations become an unavoidable element of the academic writings. In his prolific and pioneering work, Graves dedicated an entire lecture to the issue of paralysis, though he explicitly chose the term 'paraplegia' as its running head[1]. At that remote time of the 19th century, finding out that nervous injuries could follow a centripetal trajectory was highly sensitive, as Graves wrote: "When a certain portion of the extreme branches of the nervous tree has suffered an injury, the lesion is not confined merely to the part injured, but in many instances is propagated back towards the nervous centers"[1]. After marshaling several arguments that mirrored the general medical opinion of that time, paraplegia occurred due to bowel inflammation or enteritis. Nevertheless, Graves accepted that arsenical or lead poisoning might quite well be an etiological factor, with both the irritants acting directly on the central nervous system[1].

The paralysis of the lower extremities was more descriptive and detailed in the second volume of Leroy d' Étiolles work published in 1857, which was widely deemed as a reference source from his contemporaries[2]. After dedicating an entire chapter to empoisonings leading to paraplegia (with a particular emphasis on arsenical paralysis), and without avoiding the notion of 'intestinal irritation' with a copious list of causative infections in the sixth chapter of his work, the French physician spoke about an idiopathic paraplegia in the ensuing chapter of his work.

A single search on the PubMed with the term 'paraplegia' will produce more than 19 700 quotations, with the most distant one dating in 1827[3]. Earle took care of initial definition of the term in his collection of cases, and for that precise reason, he summoned several previous designations: "Hippocrates denominates all paralytic affections occurring after apoplexy,

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paraplegia. Aretaeus uses the word to denote a remission of sensation or motion in some one particular part. Boerhaave says that paraplegia is a palsy of all parts below the neck"[3].

The long list of the alleged etiological factors of non-traumatic paraplegia of an unknown origin was confusing to historical authors of the medicine of 19th century. Brown-Séquard numbered more than twelve conditions leading to this event in a part of one of his lectures. He wrote about 'cases of paraplegia' due to diseases of the uterus, the urethra, the bladder and prostate, nephritis and enteritis, as well as due to affections of lungs or pleura, diphtheria, diseases of the knee joints, irritation of the nerves of the skin and neuralgia, and even due to teething. It seems that the famous physician had his own doubts on the veracity of the factors included in the list. Therefore, he intuitively recollected all of those under the term of 'reflex paraplegia'. His work, originally published as a lecture in The Lancet in 1860, was thereafter printed in its complete form Williams and Norgate[4].

After such a disparate historical spectrum of alleged factors leading to non-traumatic paraplegia, it is obvious that the proposed medical treatments of the period actually are of a pure curiosity and largely obsolete. Graves mentioned several experiences of his own treatment through purgatives, cupping to the nape of the neck, diluents and opiates, moxae (a plant-parasitic nematode) applied along the course of the spinal column, blisters and liniments over the calf and the trajectory of the sciatica. But he concluded that 'strychnine' and 'sulphur' are the only internal remedies of benefit[1].

## 2. Classificatory attempts

Clear as it is, the term paraplegia is equivalent to a complete paralysis of the legs and the lower body. Incomplete lesions are given the denotation of paraparesis. Hippocrates was the first one to introduce the term, and his definition was given at the introductory notes. The famous physician thought that the occurrence was related with a blow of the disease, whence 'stroke'[5]. The word itself is composed from para (παρα – beside, from the Greek) and plessēin (πληγή – to strike, from the Greek).

The word itself has an ominous hint. In fact, the morbidity and disability produced from complete spinal cord lesions are exceptionally high. However, in view of continuous medical research and progress, infaust prognosis might not always be inescapable. The change of the prestigious journal titled 'Paraplegia' (published in 1963–1996) into 'Spinal cord' (since 1996 one of the journals of Springer Nature) reflects fairly well the optimistic attitude that is characterized over the last two decades.

In order to assess the severity of the neurological impairment, several scales have been proposed. Frankel scale, proposed in 1969, was a simple measure of 5-points (Table 1).

The American Spinal Injury Association (ASIA) and the International Spinal Cord Society have proposed another scale, modifying the Frankel's, and this is actually the most widely used clinical tool to quantify the severity of SCI[7]. The revised scale, known as the 'ASIA Impairment Scale', is reproduced in Table 2. Meanwhile, the international standards for the neurological classification of the SCI are reviewed and revised several times[8,9].

Other authors have suggested that relying on the sacral sparing as a criterion for complete spinal injury is more reliable than the criteria used by ASIA, which depends on the neurological level of injury and the width of the zone of partial preservation[10]. Obviously, sacral sparing of some functionality is of particular significance in view of preservation of some involuntary sphincter contractility. However, these slight classificatory changes in between sources are not conceptual, and the impairment scales correspond largely to one another. Most importantly, grading the severity of the spinal cord trauma has a clear prognostic value, since a complete injury after the initial acute phase has a poor outcome; it seems that the first 24 h is not only decisive, but sufficient to draw conclusions about the completeness or not of the irreversibility of the spinal injury[11].

## 3. Treatment: from bench to bedside

Large-scale studies have been so far mainly focused on the timeliness and dosage of methylprednisolone, whose efficacy during the acute phase of SCI is widely accepted. Three studies named National Acute Spinal Cord Injury I, II and III have already published their promising results[12–14]. High-dose dexamethasone is another glucocorticoid agent applied with some efficacy[15]. Among the disparate pharmacological options suggested and applied by different authors with some extent of efficacy, other potent glucocorticoids have been suggested (such as tirilazad mesylate), even through combining steroid therapy with local hypothermia. But GM1 ganglioside, naloxone, 4-aminopyridine, guanosine derivatives and agents with stem/progenitor cell proliferative properties (such as curcumin) have been tried as well[12–19]. Electrostimulation (alternating current stimulation) and elective neurosurgery (decompressive laminectomy) should be taken into consideration accordingly. Nevertheless, the actual focus of study has been shifted toward transplantation modalities, namely, the stem cell therapy.

Albeit not unknown to the scientific circles, stem cell therapy for SCI is a relatively new method. However, its successful application in a diversity of studies, some of which have already achieved their second phase, has raised consistent hopes[17–19]. The first issue of concern is where to find and produce enough precursors of the neurons, largely damaged during the SCI.

**Table 1**
The Frankel scale for spinal cord injury (SCI)[6].

| Frankel scale | | Characteristics |
|---|---|---|
| A | Complete | No motor or sensory function below level of lesion |
| B | Sensory only | No motor function, but some sensation is preserved below level of lesion |
| C | Motor useless | Some motor function without practical application |
| D | Motor useful | Useful motor function below level of lesion |
| E | Recovery | Normal motor and sensory function, may have reflex abnormalities |



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