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Spinal Cord Injury Related Pain: Diagnosis, Treatment, and Life Care Considerations

E. Franklin Livingstone, M.D., M.R.M.

Abstract. *The impact of spinal cord injury (SCI) is devastating and insidious, affecting every aspect of life; physical, medical, emotional and vocational. This article reviews relevant literature, discusses the author's experiences with patients, and summarizes available data. Suggestions for life care planning considerations are also offered as well as excerpts from an actual life care plan developed for a female client with SCI and chronic pain.*

The impact of spinal cord injury (SCI) is devastating, affecting every aspect of life; physical, medical, emotional and vocational. The incidence of SCI with survival long enough to reach hospital treatment has been estimated at between 32.2 and 60 cases per million population annually. However, there are significant state to state differences. Prevalence determinations likewise vary from study to study, but a conservative estimate of one quarter of a million SCI survivors seems reasonable (Stover, DeLisa, & Whiteneck, 1995). For these survivors, the direct and secondary complications of SCI affect every aspect of life with often permanent or progressive impact. The direct and secondary complications of SCI include paralysis, weakness, bowel and bladder dysfunction, spasticity, joint contractures, pressure ulcerations, behavioral and psychological maladaption, emotional turmoil and dysfunction, vocational and avocational disruption, and chronic pain (Winkler & Weed, 2004).

Chronic pain in people who have sustained SCI is a common and often difficult problem to manage. It is sometimes refractory to our catalog of treatment modalities. Incidence of mild to severe chronic persistent or intermittent pain following and related to SCI ranges from 18% to 96% (Anson & Shepherd, 1996; Demirel, Yllmaz, Gencosmanoglu & Kesiktas, 1998; Johnson, Gerhart, McCray, Menconi & Whiteneck, 1998; Putzke, Richards, Hicken & DeVivo, 2002; Siddall, Taylor, McClelland, Rutkowski & Cousins, 1999). It interferes with physical function and/or quality of life (QOL) in up to 45 % of affected SCI individuals (Cairns, Adkins & Scott, 1996). This pain, which is often a clinical conundrum, may cause increased physical disability, emotional distress, impaired functional improvement, vocational stagnation, and require significant long-term care involvements. In this author's clinical and personal experience, the majority of SCI survivors experience one or more categories of chronic pain.

Onset of post-SCI pain usually occurs in the first year after injury, however, later onset is not particularly uncommon, especially with pain above the level of the spinal cord injury. Approximately 60% report onset within the first six months after injury, and 90% within the first 48 months of injury. In some cases, the intensity and frequency may decrease with the passage of time, but lifelong affliction is the norm and progression is common. The more intractable pain is most frequently found to have onset at three or more months after the injury.

Pain descriptions include a constant dull aching, tingling, and sometimes intense burning (most often found with SCI). Pain can be radiating, intermittent, sharp, and lancinating (a piercing or stabbing type pain, most often in persons with cauda equina and other incomplete injuries). However, as previously noted, burning pain can be a complaint with both SCI and cauda equina injuries. Other pain categories include dysesthesia (an unpleasant sensation caused by normal stimuli), and allodynia (pain resulting from non-noxious stimulus to normal skin). Several factors may intensify these pain descriptions and aggravate the experience of pain, including stress, depression, anxiety, inactivity, overexertion, infections, decubiti, noxious stimuli and spasticity.

With spinal cord injury, there may be one or more sources for the development of chronic pain. Neurogenic pain generators may develop from injury to the spinal cord proper, or to the peripheral nerve rootlets leaving the spinal cord, as in segmental radiculopathy and cauda equina injury. In addition, there may be pain as a result of injury to the vertebral complex and other non-neurologic tissues. Musculoskeletal pain syndromes typically result from overuse, particularly in the upper extremities where wrists and shoulders are particularly susceptible to the increased demands placed upon them for mobility and transfer activities secondary to quadriplegia or paraplegia. Lastly, supratentorial, or psychogenic pain, may develop into a chronic pattern complicating diagnosis and treatment.

There have been a number of classification systems developed to categorize the various pain syndromes, however, clinical applications have not always been particularly useful. These categorization attempts have been predicated on location of pain, supposed pathological locus, and clinical characteristics such as description and course. For the purpose of this article, the classification system proposed by Cardenas, Turner, Warms & Marshall (2002) will be utilized. In this system, two major categories were proposed, neurologic and musculoskeletal. Neurologic pain was subdivided into four subcategories: SCI pain, transitional zone pain, radicular (peripheral nerve root) pain, and visceral pain. Musculoskeletal pain was subdivided into mechanical spine pain (pain in the back or neck affected by activity and position), and overuse pain (often above the injury level in areas of normal sensation or sometimes below the injury level in incomplete injuries). Psychogenic pain, though important in considerations of chronic pain diagnosis and treatment, may also result from mechanisms of central modulation of pain, is not included in this categorization scheme.

SCI pain is that which is experienced below the level of the spinal cord lesion and in an area of abnormal sensation. This pain syndrome has been called "phantom body pain," "central pain," "dysesthetic pain," and "diffuse pain." It is often described as tingling, burning, aching and throbbing in character, and is, in some cases, associated with allodynia. It may increase with infection (such as urinary tract infection), sudden loud noise, or jolting motions. "Phantom" sensations would be included in this neuropathic pain category. This pain may also be related to activity (reduced awareness by distraction of attention), is generally described as diffuse in extent, and is the most common form of neuropathic pain in persons with SCI.

Transitional zone pain is experienced at the level of the spinal cord lesion, at the transition between normal, uninjured tissue and the spinal cord below the level of injury. This pain syndrome is typified by being bilateral, associated with allodynia and hyperalgesia (excessive sensitivity or sensibility to pain), and is not related to position or activity. It is band-like in extent at the level of the spinal cord lesion, and has been defined as pain localized to two dermatomes (spinal levels), above or below the neurologic level of injury.

Radicular pain stems from injury to peripheral nerves at the nerve root level or in the cauda equina. This location of tissue damage is an important aspect regarding etiology of the

pain and its treatment. This pain radiates in the distribution of the involved nerve. It is most often unilateral and is affected by position and activity. Pain descriptions are quite variable, but often include intermittent, sharp, lancinating characteristics.

Visceral pain is generally experienced in the pelvis or abdominal areas. It is not related to activity or position, and is not associated with allodynia. Chronic visceral pain is relatively rare as a result of SCI, with an incidence of approximately 5%. However, as with any abdominal pain, visceral pathology must be excluded before the diagnosis can be made with any level of assurance. Thorough physical examination and laboratory studies should be completed and Computed Axial Tomography (CT) or Magnetic Resonance Imaging (MRI) studies may be necessary to rule out any structural pathology.

Mechanical spine pain occurs as a result of the actual spine injury and is localized to that injury level without radiation. It is usually bilateral and is related to position and activity, but may not be indicative of spinal instability. It is not associated with allodynia and often described as aching in character. Mechanical type pain can be experienced at the tops of rods used for spinal fixation, and may require late removal of rods after spinal fusion or stability has been achieved.

Secondary musculoskeletal overuse pain is caused by increased demands on functioning body parts which are experiencing increased physical stress due to activity. This pain is experienced above the level of the SCI in areas of normal sensation, most typically in the upper extremities, upper back and neck. It can be experienced below the level of the injury in incomplete SCI. It is always related to activity, sometimes related to position, is not associated with allodynia, and most often described as an aching pain which increases with activity and is alleviated by rest. Probably the most common examples of this are carpal tunnel syndrome and various shoulder and shoulder girdle maladies caused by overuse of the upper extremities in mobility and transfer functions. Treatment of this type of pain syndrome includes nonsteroidal anti-inflammatory drugs (NSAIDs), rest, physical medicine modalities (heat, cold, ultrasound, electrical stimulation, et al.), activity alteration, pacing, and adaptive/assistive devices and techniques, including splinting to lower biomechanical stress requirements on the affected body part. Opioids may be of benefit in some cases for short-term use, but not recommended for long-term use in this pain syndrome.

Syringomyelia (essentially a cyst in the spinal cord) is a secondary complication of SCI. It may develop late, appearing, perhaps years after the injury, and is a cause of pain and ascending (becoming more proximal), and progressive neurologic impairments. The pain produced is often described as "burning" and is, in many cases, associated with allodynia. The diagnosis is best verified by MRI, and usually requires neurosurgical intervention.

Treatment

In pain treatment, SCI associated neuropathic pain is a clinical challenge and, in general, more difficult to treat than musculoskeletal pain. No known single or multiple drug treatment regimen, physical medicine modality, alternative medicine strategy, behavioral approach, or surgical intervention has been uniformly successful in the treatment of this problem. Treatment selections are usually empirical and based on clinical judgment and experience. It is also based on identification of treatable causes of pain, such as spinal instability, spasticity, scarring, spinal cord tethering, or compression of neural tissue, as well as diagnosis of emotional or psychological factors which might exacerbate the pain syndrome, especially depression and secondary gain issues.

While opioid administration in the treatment of chronic pain syndromes is controversial and fraught with difficulties, there is support in the literature for judicial use. Methadone and other long-acting narcotic agents are preferred if opioid treatment is selected. Three studies, one a randomized controlled trial (Eidie, Stubhaug & Stenehjem, 1995), one a case series (Fenollosa, Pallares, Cervera, Pelegrin, Inigo, Giner & Forner, 1993), and the last a single blind crossover study (Glynn, Jamous, Teddy, Moore & Lloyd, 1986), show evidence supporting a cautious use of opiates for post-SCI neuropathic pain. (However, these drugs may be addictive, foster progressive tolerance and habituation, cause respiratory problems and constipation, and impair libido, general function and motivation.)

There are a number of classes of medications which have been used, mostly empirically, in the treatment of chronic post-SCI related pain. If pain is associated with muscular spasticity, use of antispasmodic medications may offer some relief. These medications include Baclofen®, Zanaflex®, Dantrium® and Valium®. Where pain is associated with overuse of functional body parts, anti-inflammatory medications, especially non-steroidal anti-inflammatory agents, may be of benefit, sometimes in combination with muscle relaxant medications, such as Flexeril®, Soma® and Skelaxin®. Antidepressant medications, such as Elavil®, may also be helpful, particularly if depression is an associated phenomenon, and may have the effect of decreasing the perception of pain. Anticonvulsant medications such as Tegretol® may reduce neurogenic pain, and Neurontin®, which has been used successfully in the treatment of peripheral neuropathy (diseases of peripheral nerves), may be of benefit and has shown anecdotal success, but has not yet been validated by controlled clinical studies (Kapadia & Harfden, 2000). Clonidine®, an anti-hypertensive medication, has shown some effectiveness in reducing post-SCI pain, unfortunately, most patients have reported significant drowsiness as an adverse side-effect, which underscores the two-edged nature of pharmaceutical treatment, in general.

Combination pharmaceutical treatment is often utilized in attempts to reduce suffering and functional impairment associated with post-SCI pain. In addition, physical medicine modalities, such as accupuncture and transcutaneous electrical nerve stimulation (T.E.N.S.), have been used with anecdotal success. But as with medication treatment in combination or separately, there is, as yet, no known treatment regimen that has been shown to be universally effective in reducing or eliminating pain and its negative impact.

Medication treatment by mouth is often supplanted with epidural administration. In this procedure, a catheter is surgically implanted to facilitate the deposition of the pharmaceutical agents in the epidural space of the spinal cord. The idea behind this process is to increase the effectiveness of the medications by targeted administration, while reducing the systemic effects of the medications, including adverse side effects. Many medications have been administered in this fashion including Morphine, Clonidine®, Baclofen® and buprenorphine. All of these treatment regimens have shown some success, however, Morphine intrathecally (epidural space) has demonstrated satisfactory pain relief in up to two-thirds of patients without developing tolerance to morphine after three years of treatment (Fenollosa, Pallares, Cervera, Pelegrin, Inigo, Giner & Forner, 1993).

When simple by-mouth medication and physical medicine treatment is inadequate, more invasive procedures may be considered. Neuromodulation techniques include implantable medication pumps with epidural catheters and spinal cord stimulation (SCS) with implantation of epidural electrodes. These techniques lend themselves to trials before final implantation and removal of the appliances and reversal to pre-implantation status. With infusion pumps and epidural catheters, various medications or combinations of medications can be tried and

changed at will to determine most efficacious treatment. With epidural SCS, different parameters of the electrical stimulation can be modulated, again to determine the most beneficial treatment. In cases where there is inadequate or no significant pain relief, these procedures are completely reversible, without residual structural damage, although one should not take lightly the possible complications of even minor surgical procedures such as bleeding, cerebrospinal fluid leaks and infection. The data suggests a relatively high rate of pain relief (at least 50 percent) immediately postoperatively, however, over time the success rate drops significantly (Shimoji, Hokari, & Kano, 1993; Meglio, Cioni, & Rossi, 1989; Gevirtz, 2004).

When all else has failed, more destructive procedures have been performed including cordotomy, myelotomy, spinal cord untethering and dorsal root entry zone (DREZ) lesioning. Cordotomy and myelotomy are neurosurgical procedures to transect the spinal cord or specific neural structures in the spinal cord. Spinal cord untethering is a procedure to eliminate scar tissue adhesions which may tether the spinal cord and/or nerve roots, which are thought to play a role in pain generation. DREZ lesioning is a technique which involves cutting, or otherwise destroying the dorsal roots of the spinal nerves as they enter the spinal cord. These dorsal roots are responsible for transmitting sensory and pain stimuli to the spinal cord where they are subsequently routed to the brain. Given the potential complications of these surgical techniques, the irreversibility of the resulting tissue damage, and the relatively weak evidence to support these procedures, recommendation routinely is unwarranted (Gevirtz, 2004). Some pain clinics now offer radio frequency rhizotomy, a much less invasive one day out patient procedure for pain management.

Life Care Planning Considerations

Life Care Planning in individuals with SCI who also have chronic pain situations is laden with many potential complications. There may be a number of associated problems such as psychological, psychiatric, emotional and behavioral idiosyncrasies, and the course of each of these concomitants may be difficult to predict with any certainty. The chronic pain syndrome itself may represent the cumulative effects of multiple cause and effect relationships affecting pain perception and central pain processing. The treatment program itself may require some fluidity and change. The actual treatment of chronic pain is a mixture of art and science and it most often requires a multi-disciplinary approach to be at all comprehensive and efficacious. The life care planner, should have, at least, some familiarity with the diagnosis and treatment of pain and associated problems.

Usually there will be one or more medications to treat the pain, but as previously noted, there may be associated problems also requiring pharmaceutical treatment such as depression, anxiety, muscle spasticity, and insomnia. At times, medication is prescribed so that another medication will be tolerated, as is the case, at times, with non-steroidal anti-inflammatory agents. In addition, these medications may need adjustment or change secondary to habituation, addiction, adverse reactions, inefficacy, or as new, more effective medications become available.

Other treatment options and regimens are available. As mentioned, physical medicine modalities such as heat, cold, accupuncture, acupressure, exercise and electrical stimulation, to name a few, have proven beneficial. Behavioral therapies including hypnosis, biofeedback, and relaxation techniques are frequently helpful in controlling or reducing pain perception and suffering. Cognitive therapies through group, family, and individual counseling have been successful in altering belief patterns and "self" concepts to aid in treatment success. As a last

resort, surgical interventions are available and perhaps, too often utilized. None of these treatment modalities provides a cure in most cases, and chronic pain (consistent pain lasting longer than six months) remains a complex and enigmatic clinical problem, to say the least.

Pain, itself, is a subjective experience, with subjective reporting and a wide variance in pain sensitivity and individual suffering. Diagnosis and treatment are also complicated by motivation, compliance and secondary gain issues. Chronic pain has insidious effects on all aspects of the pain sufferer's life, to include physical, psychiatric, emotional and spiritual. It may reduce quality of life (QOL) in many ways by interfering with participation and performance vocationally, avocationally, sexually, in relationships, and in self-care and living skills activities. Sleep deprivation is common and warrants special consideration and treatment because it negatively affects all other problems associated with chronic pain. These multitudinous consequences must be taken into account by the life care planner.

Post-SCI pain is complicated to treat, as well as it is difficult to predict and plan for. In many cases, treatment is only partially successful and some types of SCI-related pain, in certain individuals, have been largely refractory to any treatment, leading to extensive evaluation and treatment by multiple physician and non-physician professionals. Additionally, in many cases, the pain problems increase and/or multiply over time, especially with overuse syndrome in the overtaxed, functioning body parts. These factors may result in "doctor shopping" and expensive evaluation and treatment trials, often leading to more frustration and discouragement which only tends to aggravate the situation. In addition, these same difficult to prognosticate factors may lead to progressively invasive treatment procedures.

Effective treatment often requires a multidisciplinary and multimodality approach, the goals of which will encompass maximal pain relief, social, vocational and avocational reactivation, and to minimize the overall negative impact of the pain syndrome and to maximize QOL. This is most frequently attempted in the outpatient setting; however, in many cases, the likelihood of optimal success is enhanced with comprehensive inpatient treatment. Evaluations may be extensive and should include psychological and neuropsychological testing, as well as delineation of associated or concomitant psychiatric, emotional and sleep problems, maladaptive behavior patterns and secondary gain issues or malingering. The treatment team will be specified by the profile of needs of the individual and may include physical and occupational therapists, dietician, psychologist, physical medicine and rehabilitation specialist (physiatrist), psychiatrist, biofeedback therapist, orthopedist, neurosurgeon, neurologist, social worker, case manager, clergy, and vocational rehabilitation expert. As one might imagine, to coordinate a potentially large pain rehabilitation team is more manageable in the inpatient setting where environment and activities structure can also be monitored and controlled with more effectiveness than in the outpatient setting.

The best source of information and guidance in the prediction of evaluation and treatment needs is the primary pain treatment physician. However, because there are often multiple physicians involved, and frequently more than one type and location of pain, individual contacts with treating physicians are often required. It would not be unusual to construct a predicted care plan scenario based on the opinions of several treating physicians, or to structure predicted care plans for each specific type and location of pain. Teamwork and cohesiveness in goals and treatment planning and implementation are imperative to optimize pain reduction and functional outcome.

Vocational Considerations

Return to gainful employment is often used as a measure of recovery after spinal cord injury, and was, in the past, equated with the ultimate success in spinal cord rehabilitation. Unfortunately, successful return to work and vocational rehabilitation occurs in less than 50 percent of cases when all SCI cases are considered. Post-SCI employment figures vary considerably from study to study with a range from 13 to 48 percent (Trieschmann, 1988). There are many pre-injury and post-injury factors including the level and degree of neurological deficits associated with successful post-SCI employment. Paraplegics are more likely to reach employment than tetraplegics (quadriplegics), and incomplete injuries more so than complete neurologic injuries (Winkler & Weed, 2004). Other factors predicting success include younger age of injury, pre-injury education and employment success, personal motivation, and successful completion of a vocational rehabilitation program.

Chronic post-SCI pain is a "wild card" with insidious and negative impact on re-employment success. The variability of chronic pain related impairment in an individual can be significant from day to day or even within a 24-hour period, and can make adherence to daily time-structured activities difficult or impossible. The low rate of complete cure, particularly in cases with distressing, neurogenic dysesthesia, was found to be 5.8 percent by Stormer, Gerner, Gruninger, Metzmacher, Follinger, Wienke, Aldinger, Walker, Zimmermann, & Paeslack (1997), and the limited success of current treatment regimens suggests a significant inverse correlation between the extent of pain and successful vocational rehabilitation (Stormer, et al, 1997).

Sleep disturbance caused by chronic post-SCI pain alone results in significant sleep deprivation and functional impairment, and tends to exacerbate the experience of pain. Up to 77 percent of chronic post-SCI pain sufferers report frequent sleep interference caused by pain, with either difficulty getting to sleep, staying asleep, or both (Widerstrom-Noga, Felipe-Cuervo & Yezierski, 2001). Adversities such as this make adherence to inflexible work schedules unlikely, and only substantial flexibility in time structure and productivity measures will facilitate vocational success. Creativity may be necessary in development of vocational rehabilitation goals and planning. Although the specific recommendation should be left to a qualified rehabilitation counselor, in these cases, home-based self-employment may offer the best alternatives for those with an entrepreneurial motivation.

Conclusion

Life care planning for patients with SCI is complex to begin with, and the addition of a chronic pain syndrome with its many presentations, a multitude of treatment options all with limited efficacy, and the potential for progression over time, makes this planning even more challenging. The life care planner should have, at the least, a rudimentary understanding of this complex problem, and must be able to synthesize and structure predictions in a coherent and justifiable manner. Where case management has been inadequate, the life care planner may identify the fact that the client is "slipping through the cracks" of diagnosis and/or treatment, and shed light on this inadequacy to treating professionals. In this way, the life care planner may play an even more beneficial role in the progression of care and reduction of morbidity.

Case Study

The client is a 32-year-old female who sustained a complete T10-11 spinal cord injury ten years ago when she was struck from behind by a railroad train. She has had a mixed pain history, including neuropathic pain, mechanical back pain, and upper extremity pain at the shoulders and wrists related to the increased demands upon the upper extremities for mobility and transfer functions. She has had a plethora of treatment recommendations and surgical and non-surgical treatments by several physicians, and at least a score of different medication trials. She also continues to take pain medications, including narcotics. She has undergone orthopedic surgery with fusion for intra-vertebral instability, and neurosurgery for lysis of spinal cord adhesions (untethering). Yet, she continues to have significant pain, paresthesia, and sleep disturbance and may be a candidate for a medication pump with epidural catheter for narcotics by this method. Pain has become the dominant issue in her daily life. It has caused educational stagnation, misery, and exacerbates the already significant uncertainties in her future, making future care planning seem almost futile.

Currently, there are three physicians involved in diagnosis and treatment of her multiple pain complaints: a physiatrist (PM&R), a neurosurgeon, and an orthopedic surgeon. Life care planning will need to encompass the complexity of this aspect of her life to make reasonable extrapolations from current to future needs. Each of the involved physicians will bring a different perspective to these problems and will be cumulative. And the pervasive effects of pain and sleep disturbance on all tiers of function, personal, social, vocational and avocational, should be recognized and appropriately accounted.

The following includes pain-related entries from her life care plan:

Routine Future Medical Care – Physician Only			
Recommendation	**Frequency and Duration**	**Purpose**	**Expected Cost**
Physiatrist to include pain management	1 X month (avg.) to life expectancy	Monitor pain, long-term rehab. needs and reduce complications	$900/year to life @ $75/visit
Spine MRI	Every 2 years (avg.) to life expectancy	Monitor changes in spine over time	$1,000-1,600 dep. on w/ or w/out contrast
Urine toxicity tests	1 X year (avg.) to life expectancy	Monitor urine toxicity levels due to medications	$20-50 (est.) per year depending on tests ordered
Orthopedic Surgeon	Every 2-3 years (avg.) to life expectancy	Monitor spine instrumentation and hips	$80-150/visit
Spine x-rays	Same as above	Same as above	$424 (includes radiologist read fee)
Pelvis x-rays	Same as above	Same as above	$331 (includes radiologist read fee)
Trigger point injections	2 X year (avg.) to life expectancy	Pain management	$250-300/year to life @ $125-150 per injection

Projected Therapeutic Modalities			
Recommendation	**Frequency and Duration**	**Purpose**	**Expected Cost**
Physical Therapy	24 sessions (avg.) per year to life (3 X week for 4 weeks every 6 months)	Expected flare-ups	$1,560-3,600/year @ $65-150/visit
Occupational Therapy	24 sessions (avg.) per year to life (3 X week for 4 weeks every 6 months)	Expected flare-ups	$1,560-3,600/year @ $65-150/visit
Counseling: Individual/Family	1 X week for 48 therapeutic weeks per year for 2 years (2005) then 2 X month for 12 months then 1 X month for 12 months then 2 X year to life expectancy for evaluation/screening	Pain management, adjustment, education, coping, marital/sexual relations, etc.	Initial visit: $175-200 Follow-up: $150-200 per session
Peer support group for individuals with spinal cord injury	1 X week if available		$0. Typically no cost for peer group if offered through local support network.

Drug Needs ***Drugs and costs change over time and are representative of the client's current needs.*** ***Note: The implantation of a narcotics pump will change the need for pain medications listed below.***			
Recommendation	**Purpose**	**Cost per Unit**	**Cost per Year**
Oxycontin, 40 mg, 2 X day	Pain control	$299.50 for 60 tablets	$3,644/year to life
Oxycodone, 5 mg, 1 X day (avg.)	Break through pain	$30.75 for 90 capsules	$125/year to life
Valium, 10 mg, 2 X day	Spasms	$23.99 for 120 tablets	$146/year to life
Neurontin, 1800 mg, 3 X day	Nerve pain	$396 for 180 tablets	$2,409/year to life
Skelaxin, 400 mg, 2 tablets at night	Spasms	$66.25 for 60 tablets	$806/year to life
Prevacid, 30 mg, 1 X day	Stomach upset	$132.01 for 30 capsules	$1,606/year to life
Zoloft, 100 mg/night	Depression	$82 for 30 tablets	$998/year to life

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About the Author

Dr. E. Franklin Livingstone developed the desire to pursue a career as a physiatrist after a motor vehicle accident resulted in L2 level paraplegia in 1967. He is a graduate of the University of Washington Medical School, board certified in the specialty of Physical Medicine and Rehabilitation, and is currently the Director of Rehabilitation Medicine at Havasu Regional Medical Center, in Lake Havasu City, Arizona. He can be reached at 928-854-0011 or eflmd@msn.com or visit his website at http://www.doctor-livingstone.com/.