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An evidence-based review of aging of the body systems following spinal cord injury

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Abstract

Study design—Systematic review.

Objective—To systematically review evidence on aging of the body systems after spinal cord injury (SCI).

Setting—Toronto, Ontario and Vancouver, British Columbia, Canada.

Methods—Electronic databases (MEDLINE/PubMed, CINAHL, EMBASE, and PsycINFO), were searched for studies published between 1980 and 2009. The search was augmented by reviewing the reference lists of relevant papers. Non-intervention studies that were longitudinal or cross-sectional with able-bodied (AB) controls that were at minimum matched on chronological age were included for review. Levels of evidence were assigned to the study design using a modified Sackett scale.

Results—Of the 74 studies selected for inclusion, 16 were longitudinal in design. The hypothesis that SCI represents a model for premature aging is supported by a large proportion of level 5 evidence for the cardiovascular and endocrine systems, level 2, 4 and 5 evidence for the musculoskeletal system, and limited level 5 evidence for the immune system. Only a few level 4 and 5 studies for the respiratory system were found. The evidence on the genitourinary system, gastrointestinal system, and for skin and subcutaneous tissues provide level 4 and 5 evidence that premature aging may not be occurring. The evidence on the nervous system does not provide evidence of premature aging as a result of SCI.

Conclusions—Premature aging appears to occur in some systems after SCI. Additional longitudinal studies are required to confirm these findings.

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Conflict of interest
The authors declare no conflict of interest.

Keywords

spinal cord injuries; aging; body systems; longitudinal

Introduction

The literature suggests that persons with spinal cord injury (SCI) may be more susceptible to earlier age-related functional declines when compared to the able-bodied (AB) population,[1] and that SCI represents a model for premature aging.[2] Such premature aging of certain body systems has been said to occur because of additional stresses extending to physical systems beyond their ability to repair themselves.[3] Although the aging process occurs at varying rates and at different ages for each individual,[4] it is generally accepted that bodily functions reach a maximum capacity before or during early adulthood, before beginning to gradually decline. This decline is thought to commence at approximately 25 years of age when the developmental process plateaus and biological capacity has peaked.[5] This physical peak can be measured by examining the functioning of the individual organ systems (for example, cardiovascular capacity via how well the heart can pump blood) or by assessing the individual's maximum functional abilities (for example, amount of weight that can be lifted). After this peak, the body's reserve capacity of its organ systems begins to drop at a rate of 1% per year in AB persons. Thus, the average person at age 70 has about 50% of his/her capacity remaining in each organ system, which does not necessarily present a problem since all organ systems have "excess reserve" (that is, more cells, structure, and supportive tissue than is required to meet daily life needs).[6] When reserve capacity diminishes to below 40% of original functioning, however, there is greater chance of becoming injured, and/or more susceptible to infection or disease.[6] A SCI results in physiological and functional changes, and potentially accelerates bodily declines at approximately the time of injury, after which the effect of aging is said to proceed at a normal rate.[7]

Age of SCI-onset may have important consequences on different aspects of health. As there are increasing numbers of seniors incurring a SCI due to falls, a bi-modal age-of-onset distribution exists, with the prevalence of SCI peaking among individuals who are 30 and 60 years of age.[8] As a result, researchers have been able to investigate and compare age-related outcomes after SCI. For example, there are a number of studies showing that persons who incur a SCI at later ages have poorer functional outcomes than those injured at younger ages.[9–11] Within a theoretical reserve capacity model of aging that is disrupted by SCI, Adkins[7] posits that the impact of injury 'decreases the further out on the age continuum the injury occurs' (p. 5). However, if the injury occurs far enough along the continuum, then even a minimal change in rate will lower reserve capacity below 40% since capacity is already low. Further, adults with older ages of SCI-onset may have other pre-existing co-morbidities that affect outcomes compared to younger adults.[9]

Fortunately, increases in life expectancy are providing opportunities to clarify the changes to body systems resulting from SCI, aging, or both. What is clear is that physiologic systems do deteriorate with age, and this has been well documented in person with SCI.[3, 10] They

may experience upper limb extremity pain,[11, 12] rapid bone loss in the lower extremities (that is, hips and knees),[13] develop multiple risk factors for cardiovascular disease,[14, 15] experience declines in pulmonary function,[16] and have recurring problems with the genitourinary[17] and gastrointestinal[18] systems.

The breadth of aging-related issues after SCI is expansive, and there is substantial overlap from body system to body system. Indeed, difficulties in one area impacts others, resulting in compromised system functioning.[19] Presently, we have a naïve understanding what it means to live long term with SCI, but the field is now at a point where the evidence to-date can be systematically evaluated to better understand issues associated with aging following SCI. Hence, the purpose of this evidence-based review is to clarify the role of age (including age of SCI onset) and years post-injury (YPI) on outcomes, and to determine if premature aging is occurring for each physiological system.

Materials and methods

A systematic review of all relevant literature published from 1980 through to the end of December 2009 was conducted using multiple databases (MEDLINE/PubMed, CINAHL, EMBASE, PsycINFO).[20] The key word '*spinal cord injuries*' and its variants were used with the following terms: *aging, longitudinal, prospective,* and *case-control.* Reference lists of relevant articles were reviewed and authors' names that came up frequently were targeted to augment the search. The articles considered for review were English non-intervention studies that had adult (> 18 years) SCI participants with traumatic etiologies comprising at least 50% of the sample.

With the intention of addressing aging of the body systems after SCI, studies that were longitudinal (including retrospective cohort data) or prospective in design that had observations of at least 2 years or more were included for review. However, association studies were excluded. In order to address the issue of premature aging, cross-sectional studies with an AB comparison group that was minimally matched on chronological age were also included. Case studies or studies with limited age-ranges (that is, only persons in their twenties and/or early thirties, and so on) were excluded except for monozygotic twin model designs since this design provides some independence from genetic variability and aging.

After reviewing the abstracts and identifying papers for inclusion, a quality assessment was conducted on each relevant article using the Downs and Black tool.[21] This assessment tool consists of 27 questions that evaluate the study's external and internal validity (both bias and confounding). The last question was modified from a scale of 0–5 to a scale of 0–1, where a study was provided with a score of 1 if a power calculation or sample size calculation was present. Conversely, a score of 0 was assigned if there was no power calculation, sample size calculation or explanation on whether the number of subjects was appropriate. Thus, the highest score any reviewed article could receive was 28, with a higher score indicating higher methodological quality.[21] Two independent reviewers assessed the quality of the studies. Discrepancies in scores were resolved by a third reviewer. Five levels of evidence, based on a modified scale, were used to rank the data[22] (see Table 1).

Results

This search involved reviewing over 17 000 titles and 8400 abstracts. Seventy-four articles met the inclusion criteria. The articles were categorized according to seven body systems: cardiovascular and endocrine systems (n = 24), immune system (n = 2), musculoskeletal system (n = 25), respiratory system (n = 4), skin and subcutaneous tissues (n = 2), genitourinary and gastrointestinal systems (n = 16), and nervous system (n = 4). It should be noted that some articles overlap across categories. The results presented from each study primarily focus on the analyses relevant to aging, and the *P*-values reported in Tables 2–8 are those reported in the original articles.

Cardiovascular System

Fifteen studies were identified for the cardiovascular systems (see Table 2). There is level 5 evidence that plasma homocysteine levels are higher in persons with SCI (n = 835) compared to the AB population (n =14 838), with discrepancies greatest in older adults with SCI (> 50 years).[23] Elevated levels of plasma homocysteine have been shown to be a clear marker for the prediction of vascular disease, although it is unclear if it is the main cause or only an associated factor.[24, 25]

There is conflicting level 5 evidence from several studies demonstrating that persons with SCI have abnormal lipid profiles[2, 26–33] with some studies[27, 32, 33] reporting that total cholesterol/high-density lipoprotein levels, total cholesterol[33] and low-density lipoprotein[33] were higher in persons with SCI than in AB controls, while others[2, 27–29, 32] found that total cholesterol, high-density lipoproteins, and low-density lipoprotein levels were lower. It is possible that lifestyle factors may have accounted for differences across these studies, but further work is needed to clarify the role of diet and physical activity to aging with SCI.

Another study provides level 5 evidence that C-reactive protein levels are higher in men with SCI (n = 62) compared with AB controls (n = 29), which could also account for the decreases in total cholesterol, low-density lipoproteins and high-density lipoprotein levels.[29] At the same time, increases in C-reactive protein levels may also partly explain why persons with SCI are nonetheless at increased risk for accelerated atherogenesis.[32] As well, one study provided level *5* evidence that persons with SCI (n = 144) also have greater atherosclerotic burden compared with an AB reference population (n = 273) (Orakzai *et al.*[34]).

Finally, two studies provide level 5 evidence that when compared with AB controls, men with complete T6 or above paraplegia (n = 50) have an abnormal (absent) heart rate response during exercise, and men with complete tetraplegia (n = 7) have increased mean arterial blood pressure.[35, 36] These findings are indicative of altered autonomic control, and may contribute to changes in cardiovascular health.

Endocrine System

Thirteen studies were identified for the endocrine system (see Table 2). There is level 5 evidence that secretion of testosterone and human growth hormone levels are lower in persons with SCI compared with AB controls.[37–40] Level 5 evidence from two studies[37, 41]

suggests that serum insulin like growth factor 1 levels are impaired in persons with SCI compared to the AB population, and may be a sign of premature aging. There is also level 5 evidence that glucose tolerance is lower after SCI, [2, 29, 42] which concurs with level 5 evidence that diabetes mellitus occurs prematurely in men with SCI (n = 3708) compared with AB controls (n = 18 018) (Lavela *et al.*[43]). There is level 5 evidence that persons with SCI have higher levels of fat mass, and experience significantly faster rates of age-related declines of lean tissue, than in the AB population.[26, 27, 42, 44–46] Finally, there is level 5 evidence that basal and resting energy expenditures are lower in mens with SCI (n = 13) compared with their AB twin.[47]

Immune System

Two studies on the immune system after SCI (see Table 3) provide level 5 evidence that this system is compromised at both the acute and chronic stage of SCI compared to the AB population.[48, 49]

Musculoskeletal System

Twenty-five articles were identified relevant to the musculoskeletal system (see Table 4), which support the notion of premature aging in most areas with a few exceptions. There is level 4 evidence[50–52] and level 5 evidence[53–63] that there is a rapid loss of bone in the hip and lower extremities following SCI, and that this bone loss is significantly lower than the AB population. Within these studies there are also some interesting patterns found in relation to chronological age and YPI with the extent and rate of system decline. For instance, three studies provide level 5 evidence that older men and women with SCI may not experience as rapid of a decline in bone mass compared with AB controls.[57, 60, 62] Conversely, there is level 5 evidence that YPI may be more associated with bone loss after SCI than chronological age,[53, 57] therefore suggesting premature aging.

There is level 5 evidence that differences exist in bone geometric indices and in structural properties in the lower extremities of women with SCI (n = 19) compared with the AB women (n = 17) (Slade *et al.*[59]). Level 5 evidence from five studies suggests that biochemical and bone markers in persons with SCI are impaired compared to AB controls, [55, 62, 64–66] which contributes to a greater risk for fracture due to the premature development of osteoporosis. Conversely, there is level 2 (Catz *et al.*[67]) and level 5 (Chow *et al.*[54]); (Garland *et al.*[57]); (Szollar *et* al.[60–62]) evidence that premature aging does not occur in the lumbar spine after SCI. As well, one study provides level 5 evidence that persons with SCI, regardless of age or YPI, have increased thoracic kyphosis compared to AB controls.[68] However, thoracic kyphosis may also be attributable to muscle changes (that is, innervated musculature).

With regard to the upper extremities, there is level 2 evidence showing that the incidence of shoulder pain increases over time in persons with SCI.[69, 70] This is supported by level 5 evidence that upper limb pain in men with complete paraplegia who use manual wheelchairs may be attributed to longer YPI and not to chronological age.[71] However, there is also level 2 (Lal[72]) and level 5 evidence[73] that highlights chronological age as having an important influence on developing shoulder pain. Finally, there is level 5 evidence that premature aging

does not occur in hand grip strength in men with complete paraplegia and that continual manual wheelchair use may retard this aging process.[35, 71]

Respiratory System

Four studies on the respiratory system were identified (see Table 5). There is level 4 (Bach and Wang[74]) and level 5 evidence[75, 76] that sleep disordered breathing as characterized by sleep apnea, oxygen desaturation, and snoring is more prevalent in SCI populations, and that it may either increase or persist with the aging process in persons with SCI.[74] As well, one study relying on self-report found that persons with SCI (n = 408) snored more often, louder, and commenced at a younger age than AB controls (n = 339) (Biering-Sorenson F and Biering-Sorenson M[76]) which could be interpreted as premature aging. Level of injury, however, likely plays an important role given that another study found that six patients with tetraplegia (n = 16) had oxygen saturation levels below the normative range (n = 12) (Cahan *et al.*[75]). As well, there is level 5 evidence demonstrating that seated breathing patterns are compromised immediately post injury in men with tetraplegia (n = 6) compared with AB controls (n = 18) but appear to recover over time[77].

Skin and Subcutaneous Tissues

Two studies were identified on skin and subcutaneous tissues (see Table 6). There is level 2 evidence indicating that men with SCI (n = 10) have higher, albeit not significant, levels of a collagen metabolite, glu-gal Hyl, than AB controls (n = 5) (Rodigruez and Claus-Walker[78]) and level 4 evidence from a two-year study that increased excretions of glu-gal Hyl is significantly associated with development of pressure ulcers in men with SCI (n = 62) (Rodriguez and Garber[79]).

Genitourinary System

Eleven studies were identified for the genitourinary system (see Table 7). There is level 4 evidence that up until 5 YPI, there are no differences in renal functioning, at which time functioning has been noticed to decline.[80–82] One study provides level 4 evidence that repeated episodes of vesicoureteral reflux can cause kidney damage as early as four YPI in some persons with SCI (n = 32) (Lamid[83]). As well, there is level 4 evidence that renal plasma flow declines until 10 YPI after SCI (n = 1114), at which time a slight reversal occurs[81]. One level 5 study with SCI (n = 400) and AB groups (n = 287) suggests that age of onset may be an important factor related to renal functioning.[84] It was shown that those individuals with SCI under 20 years of age or older than 50 had comparable renal functioning to the AB controls, whereas persons between those ages were more likely to have impaired functioning. Finally, there is level 5 evidence that men with SCI do not appear to be at higher risk for the development of prostate cancer compared to the general population,[85–90] but when detected in persons with SCI (n = 7), the cancer may be more advanced and metastatic than in AB controls (N = 267) (Scott *et al.*[86]).

Gastrointestinal System

Five studies were identified for the gastrointestinal system (see Table 7). A 10-year longitudinal study provides level 4 evidence that persons with SCI (N = 159) do incur an

increase in constipation-related symptoms over time.[91] It may be that bowel functioning worsens over time for persons with SCI but three studies[92–94] provide level 5 evidence that level of injury plays a primary role in the extent of bowel dysfunction. As well, one study provides level 5 evidence that deterioration in bowel continence increases with age in an AB population (n = 467) but does not change in persons with SCI (n = 467) (Lynch *et al.*[95]).

Nervous System

Four studies (with SCI samples of > 70; see Table 8) provide level 4 evidence that the early onset of SCI-related pain is likely to persist over time,[69, 70, 96, 97] and that the degree of interference experienced might be impacted by age of onset.[69]

Discussion

A majority of the articles (64%) in this review were on the effects of aging with an SCI on the cardiovascular, endocrine, and musculoskeletal systems, which provided limited level 2 and level 4 evidence, and a large proportion of level 5 evidence, in support of the premature aging hypothesis of these systems. Fewer studies (5%) were found on the respiratory system, which provide limited Level 4 and 5 evidence that this system is negatively impacted by aging after SCI. Only two level 5 studies (3%) provided support for the immune system. The studies (20%) on the genitourinary and gastrointestinal systems provide limited level 4 and 5 evidence on the negative effects of aging but do not appear to suggest premature aging. Similarly, level 2 and *4* evidence (3%) for the skin and subcutaneous tissues also does not suggest premature aging. The level 4 evidence (5%) on the nervous system provides some insight on the role of age and YPI, but no evidence to support or denounce the premature aging hypothesis.

Cardiovascular and Endocrine Systems

The evidence reviewed appears to support the hypothesis that there is premature aging of the cardiovascular and endocrine systems after SCI. The predisposition to carbohydrate and lipid abnormalities is thought to be largely a consequence of extreme inactivity, and the constellation of metabolic findings (that is, hormone growth hormone deficiency, testosterone deficiency) appears to occur prematurely in persons with SCI.[2] However, some caution is warranted when interpreting the findings of studies that used standard body mass index values to predict outcomes (that is, Liang *et al.*[29]), which have been shown to be inappropriate for persons with SCI.[44] As well, all the identified studies for these systems only provided level 5 evidence that reserve capacity is compromised. Hence, higher levels of evidence are needed to provide stronger support for the hypothesis of premature aging.

Immune System

With regard to immune functioning after SCI, the identified studies indicate that the system is compromised compared with AB controls,[48, 49] suggesting reduced reserve capacity, but do not clarify whether chronological age (including age of onset) or YPI are significant factors. Given the lack of studies with large sample sizes or with longitudinal designs, further work is strongly needed to determine how aging with SCI impacts this system.

Musculoskeletal System

The musculoskeletal system provides obvious signs of reduced reserve capacity, and thus suggests premature aging. In general, the identified studies provide evidence for rapid bone loss, and particularly so in the pelvis and lower limb regions during the acute stage post-SCI.[51, 52, 55, 98] Further, these losses may be greater for older persons,[54] and women with SCI,[57] and is evident in both bone mineral density (amount of matter per cubic centimeter of bones) and content (bone mass). Bone geometric changes[50, 64] have been also been shown post-SCI, however, these changes may be independent of chronological age and YPI.[59]

There is evidence that endocrine changes may be contributing to the losses in bone density.[55, 62, 64–66] It is thought that altered bone structure and microarchitecture because of SCI[50, 56, 58, 59] leads to impaired calcium and phosphate metabolism and the parathyroid hormone-vitamin D axis.[55, 62, 64–66] These changes have been shown to contribute to premature onset of osteoporosis and increased risk for fracture in total and regional sites following SCI when compared with the AB population,[55–58, 60–63] which may be more related to YPI than chronological age.[53, 57] Age of SCI onset, however, may be an influential factor on the extent of the decline in bone loss,[57, 58, 60] as age-related factors may become less important on changes in bone mass when an individual reaches a certain chronological age threshold (that is, 60 years). At this point, other factors (that is, immobilization) affecting bone mass may become more prominent. However, there is evidence that the lumbar spine is not adversely affected by aging with SCI,[54, 55, 57, 60–62, 67] and postural changes are also independent of age and YPI.[68] The possibility that the lumbar spine becomes the primary weight-bearing region, along with immobilization, may serve to protect age-related bone loss changes to this region. This does not preclude the possibility that long-term weight-bearing on the spine could have long-term adverse effects.

With regard to the upper extremities, the shoulders appear to decline with YPI,[69, 71–73] while handgrip strength and bilateral elbow flexion appear to be spared or even improves with time.[35, 71] As well, the incidence of degenerative shoulder changes after SCI may be higher in persons with advanced age (older than 30 years) who are < 10 YPI,[72] suggesting that degenerative changes may occur earlier than previously thought.

Overall, the identified studies for this system provides us with the clearest picture of the effects of aging for persons with SCI through the support of studies with higher levels of evidence compared to the other body systems, and through lower level studies that noted age group comparisons (that is, Szollar *et al.*[60–62]).

Respiratory System

Although respiratory complications lead to significant morbidity and mortality in people with SCI,[99, 100] only a few studies were identified for this body system. In general, the incidence of sleep disordered breathing, characterized by sleep apnea and snoring, may be higher in persons with SCI than in the AB population,[75,76] and appears to increase with age in persons with tetraplegia.[74] As well, being in a seated position imposes greater stress on the respiratory system in the acute stage of SCI than the supine position, but may improve at one YPI, to levels more comparable with AB controls[77].

Overall, reserve capacity appears to be diminished but it is unclear if breathing patterns change as a result of the injury or because of aging with SCI. Although there are additional factors that can affect respiratory health long-term for individuals with SCI, there are several preventative activities that can be done to minimize the aging of the respiratory system, such as not smoking, minimizing exposure to polluted air, and controlling body weight.[4]

Skin and Subcutaneous Tissues

Pressure ulcers are common among individuals with SCI (20–30% incidence rate).[101] Although the primary reasons for cause include pressure, shearing, and/or friction due to continuous sitting, it may be that a SCI results in an increase in collagen metabolism, thus elevating susceptibility to pressure ulcers.[102, 103] As well, the presence of glu-gal Hyl, a collagen metabolite, in large concentrations in urine is indicative of the degradation of skin collagen. However, there is no evidence suggesting that glu-gal Hyl excretions increase with age after SCI[79] or are higher compared with the AB population,[78] suggesting that reserve capacity is not diminished. Although increasing age has been shown to be a risk factor for the development of a pressure ulcer among people with SCI,[104] there is limited evidence as to whether SCI exacerbates skin degradation due to aging.

Genitourinary System

Prostate cancer is one of the primary causes of death among men, yet the risk appears to be lower among men with SCI[87, 88, 90] due to impaired testosterone levels.[85, 89] Nonetheless, prostate cancer screening should be encouraged given the possibility that men with SCI who do develop prostate cancer may have poorer outcomes than AB men.[86]

The evidence[80–82] indicates that while renal functioning exhibits some significant declines at approximately 5 YPI, the type of bladder management used by persons with SCI may not be a strong contributor to this decline. It may also be that persons between the ages of 20 and 50 experience a disruption in biological capacity in this system during the acute phase of SCI. More work regarding age of SCI onset and the genitourinary system is needed to help determine the impact of aging. Overall, the evidence does not provide support that this system is prematurely aging following SCI.

Gastrointestinal System

Neurogenic bowel may also compound aging after SCI,[4] but some studies did not provide details of the role of age in either the SCI or AB control groups.[92] Although YPI may not play a significant role, it does appear that constipation-related problems do increase over time in persons with SCI, and suggests that attention to bowel symptoms should be incorporated into routine follow-up procedures and education.[3] Similar to the genitourinary system, the evidence on the gastrointestinal system does not provide any evidence of premature aging.

Nervous System

With regard to the nervous system, the only studies that were identified were those related to chronic pain. The clearest finding from these studies is that the presence of pain at an earlier time point after SCI appears to be the best predictor of future pain, and that this is likely

does not change significantly over time.[69, 70, 96, 97] In general, there is a continued dearth of knowledge regarding the aging SCI nervous system.

Summary

The majority of studies for all the systems provide some important findings regarding the role of chronological age (including age of SCI onset) and YPI, but there is still lack of clarity on how all of these factors affect (individually and in combination) the individual living with SCI over time, and further work is needed to determine if SCI is indeed a model for premature aging across all body systems. As noted, the studies from the musculoskeletal system provide the strongest levels of evidence of premature aging, and even do so with lower levels of evidence by providing age comparisons within studies between SCI and AB samples. Efforts should be made to do the same for prospective studies for other body systems as well. Overall, it appears that the field of aging with SCI has yet to make significant advances since many of the issues and questions raised over 15 years ago[4] are still relevant today. Although somewhat discouraging, the dearth of knowledge in some areas highlights research opportunities that will help to resolve current challenges, and more importantly, provide information to fill many existing gaps.

Limitations

Information on aging with SCI not published in English may have influenced our findings but were excluded from this review. As well, some articles with relevance may have been missed if aging was not the primary focus.

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Table 1

Modified levels of evidence

Evidence level	Description
Level 1	Not applicable given there are no studies with a design that is equivalent to a randomized controlled trial.
Level 2	Longitudinal studies that include a control group (for example, AB group) as they are considered cohort studies where one group is exposed to a particular condition (in this case, a SCI).
Level 3	Longitudinal studies which include historical controls (from chart review or database).
Level 4	Longitudinal studies including at least a baseline and follow-up evaluation (at least equivalent to before-after studies).
Level 5	Cross-sectional studies utilizing both individuals with SCI and AB controls at one point in time.

Abbreviations: AB, able bodied; SCI, spinal cord injury.

Table 2

Cardiovascular and endocrine systems

Articles	Methods	Results
Bauman *et al.*[23] USA D and B = 13 *N* = 15 683 Cross-sectional with AB controls	723 men and 122 women with SCI; mean age 38 ± 11 years, mean YPI 12 ± 9 years. Comparison of levels of PH with AB reference population (*n* = 14 838). Outcome measure: PH.	Older group with SCI (> 50 years) had ↑ mean PH ($P < 0.05$) than the younger age group. Group with SCI had ↑ levels of PH than control group.
Bauman *et al.*[26] USA D and B = 9 *N* = 82 Cross-sectional with AB controls	34 men with SCI; mean age 50 ± 2 years; mean YPI 11 ± 2 years. Comparison of BMI and PL with AB controls (*n* = 48) age and gender matched. Outcome measure: PL; BMI.	Group with SCI had ↑ levels of PL ($P < 0.005$) than the control group. No significant differences in BMI between SCI and control groups.
Bauman *et al.*[27] USA D and B = 14 *N* = 623 Cross-sectional with AB controls	234 men and 86 women with SCI; mean age 41 ± 0.62 (20–77 years); mean YPI 15 ± 0.52 (1–57 years). Comparison of serum lipid profiles with AB controls (*n* = 303), age, gender, ethnicity, and activity level matched. Outcome measure: serum TC; TGs; serum HDL-c; density LDL-c; BMI.	Group with SCI had ↓ TC ($P < 0.0001$), TG ($P < 0.05$), HDL-c ($P < 0.0005$), LDL-c ($P < 0.0001$), and ↑ TC/HDL-c ratio ($P < 0.01$) than the AB control group. The AB control group had ↑ BMI compared with the group with SCI ($P < 0.0001$), but the estimated per cent body fat was ↑ in the group with SCI ($P < 0.0001$).
Zlotolow *et al.*[28] USA D and B = 11 *N* = 80 Cross-sectional with AB controls	28 men with paraplegia, mean age 48 ± 2 (25–65 years); YPI ≥1.5 years. Comparison of diet, BMI, and serum lipid levels with AB controls (*n* = 52), age and gender matched. Outcome measure: immunoassay methods; serum levels of TC, HDL and TGs.	No differences in BMI, total caloric or cholesterol intake between SCI and AB control groups. Serum HDL-c ↓ ($P < 0.0001$) compared with AB controls. Total caloric intake ↓ with age ($P < 0.0005$) in AB controls but not SCI group.
Orakzai *et al.*[34] USA D and B = 10 *N* = 355 Cross-sectional with AB controls	67 men and 15 women with SCI; mean age 49.7 ± 12 (20–90 years); mean YPI 19.7 ± 10 years. Comparison of the burden of atherosclerosis with AB controls (*n* = 273), age, gender, ethnicity and risk factor matched. Outcome measure: electron beam-computed tomography; immunoassay methods.	Mean calcium score of the SCI group was ↑ ($P < 0.0001$) than AB controls. Prevalence of CAC was greater in persons with SCI ($P < 0.05$) than in AB controls. CAC score was also greater ($P < 0.01$).
Wang *et al.*[32] Taiwan D and B = 12 *N* = 91 Cross-sectional with AB controls	62 men with complete SCI; mean age 28.0 ± 9.7 (16.2 – 59.1 years); mean YPI 11.8 ± 7.0 (1.2–27.7 years). Comparison of serum levels of markers of inflammation (CRP interleukin-6, and soluble CD40 ligand) and endothelial activation (endothelian-1, slCASM-1 and sVCASM-1 to AB controls (*n* = 29), age and gender matched. Outcome measure: immunoassay methods.	Compared with AB controls, group with SCI had ↓ body weight ($P = 0.017$), BMI ($P = 0.044$), and serum albumin and creatinine levels ($P < 0.001$). Group with SCI had ↓ LDL-c ($P = 0.048$), ↓ HDL-c ($P < 0.001$), and ↑ TC/HDL-c ratio ($P < 0.001$), and a trend toward ↑ insulin levels than AB controls. Group with SCI had ↑ serum levels of CRP ($P < 0.001$), interleukin-6 ($P < 0.001$), endothelin-1 ($P < 0.001$), and sVCAm-1 ($P < 0.001$) than AB group.
Yamamoto *et al.*[36] Japan D and B = 10 *N* = 14 Cross-sectional with AB controls	7 men with complete tetraplegia; mean age 41 ± 10.0 (33 – 58 years); mean YPI 13.7 ± 3.4 (9–18 years). Comparison of blood pressure, heart rate, and hormonal changes during 2 min of sustained contraction with AB controls (*n* = 7), age and gender matched. Outcome measure: radioimmunoassay methods; pressure transducer; electrocardiogram.	Group with SCI had no changes in heart rate during exercise, whereas AB controls did change ($P < 0.05$). Blood pressure ↑ ($P < 0.05$) in both groups.
Petrofsky and Laymon[35] USA D and B = 13 *N* = 100	50 men with complete paraplegia; four age groups (20 – 30 years, 31 – 40 years, 41–50 years, 51–65 years); YPI range 3–10 years. Comparison of blood pressure and heart rate during isometric exercise and at rest (leg and arms) with AB controls (*n* = 50), age, gender and height matched.	Group with SCI had a larger change in blood pressures both at rest and during leg exercise ($P < 0.05$). Heart rate during handgrip exercise was normal for both SCI and AB groups, but was absent in the SCI group during the leg exercise.

Articles	Methods	Results
Cross-sectional with AB controls	Outcome measure: auscultation; electrocardiogram.	
Bauman and Spungen[2] USA D and B = 12 *N* = 150 Cross-sectional with AB controls	50 men with tetraplegia; mean age 51± 2 years; mean YPI 19 ± 2 years; 50 men with paraplegia; mean age 47 ± 2 years; mean YPI 17±2 years. Comparison of carbohydrate and lipid metabolisms with AB controls (*n* = 50) age, gender, and BMI matched. Outcome measure: mean plasma glucose and insulin values; serum lipid levels; OGTT.	82% of controls had normal oral glucose tolerance vs 38% of those with tetraplegia, and 50% of those with paraplegia. 22% of SCI were diabetic vs 6% of controls. Subjects with SCI develop carbohydrate disorders at younger ages. Group with SCI had ↑ mean glucose and insulin values during OGTT compared with controls ($P < 0.05$). Serum lipid levels in subjects with SCI showed a ↓ HDL-c level.
Bauman *et al.*[41] USA D and B = 10 *N* = 32 Cross-sectional with AB controls	16 men with SCI; mean age 45 ± 3 years; mean YPI 19 ± 3 years. Comparison of growth hormone response to hormone (hgH) release; intravenous infusion of arginine hydrochloride (30 g per subject over 30 min), with AB controls (*n* = 16), age, gender, and BMI matched. Outcome measure: plasma hgH release; plasma IGF-I.	Mean hGH responses at 30 and 60 minutes were ↓ in the group with SCI than in the control group ($P < 0.01$; and $P < 0.05$ respectively). Mean plasma IGF-I levels were ↓ in SCI subjects < 45 years old than in AB controls ($P < 0.05$). ↓daily physical activity depresses hGH/IGF-I axis in younger individuals with SCI.
Demirel *et al.*[33] Turkey D and B = 12 *N* = 121 Cross-sectional with AB controls	53 men and 16 women with SCI (6 non-trauma); mean age 33.9 ± 11.37 (10–70 years); mean YPI 16 ± 10 (1–41 years). Comparison of standard risk factors for CHD with AB controls (*n* = 52), age and gender matched. Outcome measure: BMI, diastolic blood pressure, immunoassay methods.	Impaired fasting glucose ($P < 0.001$), diabetes mellitus ($P = 0.04$), hyperuricemia ($P = 0.001$), high TC ($P < 0.001$), low LDL-c ($P < 0.001$), low HDL-c ($P < 0.001$), high TC/HDL ($P < 0.001$), LDL/HDL ratios were more common in persons with SCI ($P < 0.001$) than in the AB group, while positive family history was more common in the AB control group ($P < 0.001$).
Shetty *et al.*[40] USA D and B = 12 *N* = 160 Cross-sectional with AB controls	41 men with tetraplegia; mean age 40.9 ± 1.53 (24–66 years); mean YPI 11.5 years. Comparison of plasma growth hormone/SmC axis with AB controls (*n* = 119), age and gender matched. Outcome measure: radioimmunoassay methods.	SmC was ↓ ($P < 0.007$) in group with SCI than AB controls. Inverse relationship between SmC level, and ↑ age in both groups. Severe inactivity or SCI may cause hyposomatomedinemia, which could contribute to ↓ lean body mass and muscle atrophy, ↑ risk for pressure sore formation and osteoporosis post-SCI.
Liang *et al.*[29] USA D and B = 11 *N* = 370 Cross-sectional with AB controls	185 men with SCI; mean age 39 ± 10.4 years; mean YPI 11.7 (range 1–40.4 years). Comparison of prevalence rates of metabolic syndrome with AB controls (*n* = 185), age, gender, and race matched. Outcome measure: BMI; blood pressure; TC, and low HDL (H and LDL); elevated glucose; TG.	Group with SCI had ↓ HDL ($P < 0.01$), TG ($P < 0.05$), glucose ($P < 0.001$), TC ($P < 0.001$), and LDL ($P < 0.001$).
Jones *et al.*[42] New Zealand D and B = 9 *N* = 40 Cross-sectional with AB controls	20 men with SCI; mean age 33 ± 2 (16–52 years); mean YPI 10.3 ± 1.8 years. Comparison of prevalence of metabolic syndrome with AB controls (*n* = 20), age, gender, height, weight, and activity matched. Outcome measure: lean and fat mass assessed by DEXA densitometer; plasma glucose and insulin; TC, HDL; OGTT.	55% of the group with SCI met the criteria for metabolic syndrome, whereas none of the controls did.
LaVela *et al.*[43] USA D and B = 14 *N* = 21 726 Cross-sectional with AB controls	741 veterans (98.2% men) with SCI/D and diabetes; mean age 64.1 (range < 40 to 70+ years); mean YPI 23.9 years; 2 967 veterans with SCI/D (96.8%) and no diabetes; mean age 59.2 years; mean YPI 23.8 years. Comparison of prevalence rates of diabetes mellitus with AB populations: 1 342 veteran AB controls (range < 40 to 70+ yrs); 16 676 General population AB controls (range < 40 to 70+ years). Outcome measure: BRFSS	Diabetes prevalence ↑ among veterans with SCI/D compared to general population ($P < 0.0001$), but similar to other veterans. For those 45 to 59 years of age, diabetes prevalence was ↑ in veterans with an SCI/D.
Tsitouras *et al.*[37] USA D and B = 9 *N* = 36 Cross-sectional with AB controls	20 men with SCI; mean age 42 ± 2 years; mean YPI 15 ± 2 years. Comparison of serum growth hormone and T with AB controls (*n* = 16), age and gender matched. Outcome measure: serum T; Plasma hGH; Plasma IGF-I levels.	SCI is associated with impaired secretion of both T and hGH (not the result of aging). Duration of injury appears to have an adverse effect on serum T.

Articles	Methods	Results
Huang *et al.*[30] China D and B = 10 *N* = 50 Cross-sectional with AB controls	25 men with SCI; mean age 35.4 (18–55 years); mean YPI 7.5 (1.1–15.8 years); Comparison of hypothalamus-pituitary-adrenal axis with AB controls (*n* = 25), age and gender matched. Outcome measure: radioimmunoassay methods	Cortisol response to corticotropin-releasing hormone was ↓ ($P < 0.01$) in SCI group, but differences disappeared if correction was made for baseline values.
Wang *et al.*[38] China D and B = 9 *N* = 63 Cross-sectional with AB controls	63 men with SCI; mean age 31.2 (18–44 years); mean YPI 6.2 (8–months 20 years). Comparison of hormone patterns of gonadotropin and T with AB reference population, age and gender matched. Outcome measure: radioimmunoassay methods	7 persons with SCI had ↓ serum triiodothyronine below reference level, and 8 cases had low serum T. 17 persons with SCI had hyperprolactinemia, and 9 cases had elevated serum T level. 6 persons with SCI had elevated serumfollicle-stimulating hormone and 4 cases had elevated LH.
Huang *et al.*[31] China D and B = 14 *N* = 60 Cross-sectional with AB controls	30 men with SCI; mean age 31.4 (17.4–43.9 years); mean YPI 5.9 (.9–14 years). Comparison of pituitary-testicular and pituitary thyroid axes with AB controls (n = 30), age, and sexually active matched matched. Outcome measure: endocrinologic studies, LH; radioimmunoassay, triiodothyronine (T3).	4 persons with SCI had low levels of T3, 1 with ↑ serum follicle-stimulating hormone, 8 with ↑ serum T levels, and 11 with ↑ serum prolactin levels. Compared with AB controls, persons with SCI had ↑ LH responses, with 8 having exaggerated or prolonged LH responses.
Cheville and Kirshblum[39] USA D and B = 15 *N* = 60 Cross-sectional with AB controls	29 men and 1 woman; mean age 59 (22–82 years); mean YPI 24 (2–50 years). Comparison of thyroid function and to determine the incidence and clinical prevalence of LT3S, with AB controls (*n* = 30), age and gender matched. Outcome measure: immunoassay methods	Mean triiodothyronine (T3) levels ($P = 0.0001$) and thyroxin (T4) levels ($P = 0.02$) were ↓ in group with SCI. T3 resin uptake levels were ↑ ($P = 0.0001$) in group with SCI.
Bauman *et al.*[47] USA D and B = 11 *N* = 26 Cross-sectional with AB controls	AB twins of 13 men with SCI; mean age 37 ± 8 years; mean YPI 15 ± 9 years. Comparison of energy expenditure and FMM with monozygotic twin. Outcome measure: BEE and REE by indirect calorimetry; FFM and FM assessed by dual-energy X-ray absorptiometry; TBK.	Twin with SCI had ↓ BEE ($P < 0.005$) and REE ($p < 0.05$) than AB twin. FM was equivalent between groups, but ratios of FM to FMM and FM to TBK were ↓ ($P < 0.05$) in twins with SCI.
Spungen *et al.*[46] USA D and B = 8 *N* = 16 Cross-sectional with AB controls	AB twins of 8 men with complete paraplegia; mean age 40 ± 10 (25–58 years); mean YPI 16 ± 9 (3–26 years). Comparison of body composition differences with monozygotic twin. Outcome measure: BMI; lean and FM assessed by DEXA densitometer.	Twin with SCI had ↓ of total body lean mass ($P < 0.05$) compared with AB twin, and was found to be independent of age, at a rate of 3.9 ± 0.2kg per 5-year period of paralysis ($P < 0.005$). Group with SCI had ↑ total body FM ($P < 0.05$).
Jones *et al.* 2003[44] New Zealand D and B = 11 *N* = 19 Cross-sectional with AB controls	19 men with SCI; mean age 34 ± 8 (16–52 years); mean YPI > 1 year. Comparison of BMI and adiposity with AB controls (*n* = 19), age, gender, height, and weight matched. Outcome measure: BMI; total body and regional lean tissue and FM assessed by DEXA densitometer.	BMI was similar in both groups but total body lean tissue mass was ↓ ($P < 0.001$) whereas total body FM was ↑ ($P < 0.05$) in group with SCI. Body fat percentage was ↑ ($P < 0.01$) in group with SCI.
Nuhlicek *et al.*[45] USA D and B = 10 *N* = 37 Cross-sectional with AB controls	37 men, 19 with quadriplegia; 18 with paraplegia; age range 19–49 years. Comparison of body composition between control and groups of different SCI injury levels with AB controls (*n* = 10), age and gender matched. Outcome measure: anthropometry; TBW; predicted ECW; LBM and body cell mass BCM; ECM and ECW.	Diminishing TBW, ECW, LBM, BCM, and muscle cell mass, and ↑ fat mass with higher spinal lesions. No change in total body weight, ECM or ECW.

Abbreviations: AB, able-bodied; BCM, body cell mass; BEE, basal energy expenditure; BMI, body mass index; BRFSS, behavioral risk factor surveillance system; CAC, coronary artery calcium; CHD, coronary heart disease; CRP, C-reactive protein; D and B, Downs and Black Score; DEXA, dual-energy X-ray absorptiometry; ECW, extracellular water; ECM, extracellular mass; FFM, fat free mass; FM, fat mass; HDL, high-density lipoprotein; HDL-c, HDL cholesterol; hGh, human growth hormone; IGF-I, insulin-like growth factor; LBM, lean body mass; LDL, low-density lipoprotein; LDL-c, lipoprotein cholesterol; LH, luteinizing hormone; LT3S, low T3 syndrome; OGTT, oral glucose tolerance test; PH, plasma homocysteine; PL, plasma leptin; REE, resting energy expenditure; SCI, spinal cord injury; SCI/D, SCI or disorder; SmC, somatomedian C; slCASM-1, soluble intercellular adhesion molecule-1; sVCASM-1, soluble vascular cell adhesion molecule-1; T, testosterone; TBP, total body potassium; TBW, total body water; TC, total cholesterol; TG, triglyceride; YPI, years post-injury.

Table 3

Immune system

Article	Methods	Results
Campagnolo *et al.*[48] USA D & B = 11 *N* = 10 Cross-sectional with AB controls	4 men and 1 woman with complete tetraplegia; mean age 36.2 (20–69 years); mean YPI 33.8 (7–120 months). Comparison of an immunologic parameter, and psychological well-being with AB controls (*n* = 5), age and gender matched. Outcome measure: lymphocyte proliferation assay; natural killer cell cytotoxicity assay; cell counts; Ilfeld psychiatric symptom index.	No difference in cytometry, depression or stress. Persons with SCI had significant suppression in lymphocyte balstogenic response for the three mitogens tested (pokeweed, *P* = 0.039; conconavalin, *P* = 0.038; phytohemagglutinin, *P* = 0.0008).
Campagnolo *et al.*[49] USA D & B = 12 *N* = 46 Cross-sectional with AB controls	11 men and 17 women; for persons with tetraplegia, mean age 29 (19–51 years), mean YPI 56.6 months; for persons with paraplegia, mean age 32.6 (21–50 years), mean YPI 38.6 months. Comparison of pituitary and adrenal function with AB controls (*n* = 18), age and gender matched. Outcome measure: immunoassay methods.	Plasma cortisol and DS were ↑ (*P* = 0.06, and *P* = 0.05, respectively) in persons with SCI. When examined within level of injury, no differences on mean plasma cortisol emerged, but persons with tetraplegia had ↑ (*P* = 0.05) levels of mean plasma DS than AB controls.

Abbreviations: AB, able-bodied; BMI, body mass index; D and B, Downs & Black Score; DS, dehydroepiandrosterone sulfate; SCI, spinal cord injury; YPI, years post-injury.

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Table 4

Musculoskeletal system

Article	Methods	Results
Catz *et al.*[67] Israel D & B = 7 *N* = 29 Longitudinal	12 men and 1 woman; mean age 37 ± 5 years. (24–67 years) at injury; mean YPI 19 ± 3 years. 3 persons had non-trauma etiologies and 1 had an unknown etiology. Lumbar spine dimensions assessed twice over a 10-year interval. Comparison with AB controls (*n* =16). Outcome measure: lumbar AP radiographs.	The IALS dimensions found in the follow-up radiographs were similar to those taken 10 years earlier ($P > 0.05$).
Kiratli *et al.*[58] USA D & B = 11 *N* = 434 Cross-sectional with AB controls	239 men and 7 women with SCI; age range 21–78 years; YPI range 0.1–51 years. Comparison of BMD throughout the femur and geometric properties at the femoral midshaft with AB controls (*n* =188), age and gender matched. Outcome measure: DEXA; radiographs.	SCI group had ↓ BMD ($P < 0.0001$) in all femoral regions (27, 25, and 43% for femoral neck, midshaft, and distal femur, respectively). Group with SCI were ↓ ($P < 0.0001$) in cortical area of femoral midshaft.
Garland *et al.*[57] USA D& B = 11 *N* = 48 Cross-sectional with AB controls	31 women with complete SCI; mean age 43.9 ± 19.7 (20 – 77 years); mean YPI 16.9 ± 7.7 (2–40 years). BMD measured from lumbar spine, hip, and knee. Comparison with AB controls (*n* =17), age and gender matched. Outcome measure: DEXA.	BMD of spine in youngest (≤ 30 years), middle (31–50 years.), and oldest (50 >) SCI groups were 98, 108, and 115% of the densities of respective AB control groups ($P < 0.0001$). BMD of spine of oldest SCI group was equal to youngest AB control group. Mean loss of BMD in the knee in youngest, middle, and oldest SCI groups was 38, 25, and 25% compared with AB control group ($P < 0.0001$).
Vlychou *et al.*[63] Greece D & B = 11 *N* =149 Cross-sectional with AB controls	33 men and 24 women with paraplegia; mean age 37.8 (21–66 years); YPI range 6 months-27 years. Comparison of BMD of the proximal and distal forearm, the femoral neck, the greater trochanter, and Ward's triangle with AB controls (*n* =92), age and gender matched. Outcome measure: DEXA.	Group with SCI had ↓ BMD of femoral neck ($P < 0.001$ – male, $P < 0.001$ – woman), greater trochanter ($P < 0.001$ and $P = 0.001$), and Ward's triangle ($P = 0.001$ and $P = 0.005$). Among men, 23.3% ↓ in femoral neck, 22.5% ↓ in greater trochanter, and 20.8% ↓ in Ward's triangle compared to AB controls. In women, ↓ were 24.1%, 24.3%, and 24.2%.
Szollar *et al.*[60] USA D & B = 11 *N* = 204 Cross-sectional with AB controls	135 men with SCI; mean age 48 ± 8 (20–78 years); YPI range 0–59 years. Comparison of BMD of the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter with AB controls (*n* =69), age and gender matched. Outcome measure: DEXA.	Lumbar spine BMDs of the 40- to 59-year old and the 60+ patients were ↑ ($P < 0.012$) than the AB control group. Femoral region BMDs of the 20- to 39-year old and 40- to 59-year old patients were all ↓ ($P < 0.027$) than the AB control group. Hip region BMD loss occurred starting at 1 YPI, plateaus at 19 YPI and then improves. Spine BMD in patients never ↓ significantly and started ↑ as YPI ↑. Femoral neck and Ward's triangle BMDs ↓ after 1 YPI. After 19 YPI, slight ↑ in both regions.
Szollar *et al.*[61] USA D & B = 13 *N* = 355 Cross-sectional with AB controls	263 men with SCI; mean age 48.8 ± 1.3 (20–78 years); YPI range 0.8 to 53 years. Comparison of BMD of the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter with AB controls (*n* = 92), age and gender matched. Outcome measure: DEXA.	Lumbar spine BMD was stable with a nonsignificant ↓ in persons with tetraplegia at 1–5 YPI in the 20–39 year old group. Lumbar spine BMD maintained in all other SCI groups, increasing with age, regardless of age at injury or level of injury. Persons injured <1 year had comparable BMD to AB controls. Persons aged 20–39 years old who were injured >1 YPI had ↓ ($P < 0.01$) BMDs in femoral region than AB matched controls and 20- to 39-year olds injured <1 YPI.
Chow *et al.*[54]; United Kingdom D & B = 9 *N* = 31 Cross-sectional with AB controls	19 men and 12 women with SCI; age range 19–60 years; mean YPI 5.87 ± 10.21 (5 wks–36 years). Comparison of BMD) of right heel, lumbar spine, and proximal femur region (femoral neck, Ward's triangle, trochanteric and inter-trochanteric), and of bone structure (stiffness), with AB reference population, age and gender matched. Outcome measure: DEXA; Achilles USBD.	Ultrasonic properties at the calcaneus were ↓ ($P < 0.05$) in group with SCI. After 1 YPI, BMD in femoral neck ↓ ($P < 0.05$) in group with SCI compared with AB reference population.

Article	Methods	Results
Bauman *et al.*[53] USA D & B = 11 *N* = 16 Cross-sectional with AB controls	8 men with paraplegia; mean age 40 ± 10 (25–58 years); mean YPI 16 ± 9 (3–26 years). Comparison of total and regional BMC and BMD with monozygotic twin. Outcome measure: DEXA.	Twins with SCI had ↓ total- body BMC ($P < 0.001$) compared with AB twin controls, with legs ($P < 0.0001$) and pelvis ($P < 0.0001$) being predominant sites for loss in BMC and BMD. Duration of SCI, and not age, was associated to degree of bone loss in twin with SCI.
de Bruin *et al.*[50] Switzerland D & B = 13 *N* = 12 Longitudinal	12 men with SCI; mean age 32.4 ± 9 (23–50 years) at follow-up. Structural and geometric properties of tibia and cortical bone at 5 weeks post-injury and at approx. 2 YPI. Outcome measure: PQCT, bone stiffness measurement device.	Trabecular and cortical bone, and geometric properties of tibia bone ↓ ($P < 0.05$) within 2 YPI. Phase velocity propagation changed in swing tibia bone in 3 participants within 2 YPI.
de Bruin *et al.*[51] Switzerland D & B = 12 *N* =10 Longitudinal	9 men and 1 woman with SCI; mean age 40.9 ± 19.7 (19–81 years) at follow-up. Trabecular and compact BMD of tibia and radius at 5 weeks post-injury and at approx. 3 ½ YPI. Outcome measure: PQCT	Trabecular tibia and compact bone ↓ ($P < 0.05$) within 3.5 YPI No changes in radius trabecular bone were observed. Patterns suggest no steady state of bone BMD following 3 YPI.
Eser *et al.*[56] Switzerland D & B = 14 *N* = 110 Cross-sectional with AB controls	89 men; mean age 41.5 ± 14.2 (10–65 years); mean YPI 29.3 ± 12.5 (2 months-50 years). Comparison of BMD of distal epiphyses and midshafts of femur, tibia, and radius with AB controls (*n* =21), age and gender matched. Outcome measure: PQCT.	Group with SCI had ↓ BMD ($P < 0.0001$) than the AB control group.
Frey-Rindova *et al.*[52] Switzerland D & B = 14 *N* = 29 Longitudinal	27 men and 2 women with SCI; age range 19 – 57 years. Trabecular and cortical BMD assessed within 1, at 6 at 12, and at 24 months post-injury. Outcome measure: PQCT.	Trabecular BMD of radius and ulna ↓ in persons with tetraplegia at 6 months (radius 19% less, $P < 0.01$; ulna 6% less, $P < 0.005$), and at 12 months (radius 28% less, $P < 0.01$; ulna 15% less, $P < 0.05$) post-injury. Cortical BMD of radius and ulna ↓ in persons with tetraplegia at 12 months (radius 3% less, $P < 0.05$; ulna 4% less, $P < 0.05$) post-injury. Trabecular BMD of tibia was ↓ 6 months (5% less, $P < 0.05$), and 12 months (15%, $P < 0.05$) post-injury.
Szollar *et al.*[62] USA D & B = 11 *N* = 238 Cross-sectional with AB controls	176 men with SCI; mean age 41.2 (20–59 years); YPI range 0.8 to 34 years. Comparison of BMD of the lumbar spine, femoral neck, Ward's triangle, and the greater trochanter and comparison of serum levels of calcium, calcitonin, biochemical markers of bone formation, and parathyroid hormone (PTH) with AB controls (*n* =62), age and gender matched. Outcome measure: DEXA; immunoassay methods.	Spine BMD remained stable above fracture threshold in the 20- to 39-year. and in the 30- to 49-year age groups. In all groups, there was progressive ↓ in BMD at proximal femur, and began 1–9 YPI. For the 20- to 39-year. age group, this was significant for all three areas. For the 30- to 49-year. age group, this progressed at a slower rate, reaching threshold at 10–19 YPI for all three areas. PTH levels remained below the reference range, with a slight gradual ↑ after 1 YPI. Results suggest parathyroid dysfunction-related osteoporosis.
Finsen *et al.*[64] Norway D & B = 11 *N* = 38 Cross-sectional with AB controls	19 men with SCI; median age at injury 20 (15–64 years); median YPI 4 (7 months–33 years). Comparison of BMD of lower and upper extremities, and of biochemical and bone markers with AB controls (*n* =19), age and gender matched. Outcome measure: Gambro photonabsorption scanner; radioimmunoassay techniques.	SCI group had ↓ in metaphysis (45%; $P = 0.0001$) and diaphysis (26%; $P = 0.0001$) of tibia, while a barely significant difference of distal forearm was detected (diaphysis; $P = 0.0418$; metaphysic; $P = .1611$). SCI group had ↓ levels of serum creatinine ($P = 0.0001$), and ↑ levels of alanine aminotransferase ($P = 0.007$), serum phosphate ($P = 0.014$), follicle stimulating hormone ($P = 0.016$), and SHGB ($P = 0.009$). Total testosterone was equivalent but when divided by SHGB, ↑ ($P = 0.011$) in group with SCI.
Vaziri *et al.*[65] USA D & B = 9 *N* = 54 Cross-sectional with AB controls	40 men with SCI; age range 25 – 69 years; YPI range 3 – 50 years; Comparison of serum PTH, calcitonin, vitamin D (calcitriol), 25 hydroxy (OH) vitamin D, 1,25 $(OH)_2$, ionized calcium (Ca++), and phosphorous with AB controls (*n* =14), age and gender matched. Outcome measure: immunoassay methods.	Plasma PTH was ↓ in group with SCI ($P < 0.001$) compared with AB controls, despite equivalent concentrations of Ca++. Plasma calcitrol was ↓ in group with SCI ($P < 0.05$) compared to AB controls, and ↓ in persons with tetraplegia vs those with paraplegia ($P < 0.05$).

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Article	Methods	Results
Dauty *et al.*[55] France D & B = 10 *N* = 62 Cross-sectional with AB controls	31 men with SCI; mean age 36 ± 12.3 (18 – 60 years); mean YPI 6 (6 months–19 years). Comparison of supra- and sublesional BMD and BMC, and of blood and urine samples that included phosphocalcic parameters with determination of urinary hydroxyproline and deoxypyridinoline with AB controls (*n* =31), age and gender matched. Outcome measure: dual-photon absorptiometry; immunoassay methods.	SCI group had a ↓ ($P < 0.0001$) of sublesional BMD of 41% compared with AB controls. This loss of mass is ↑ at the distal femur (−52%) and proximal tibia (−70%). SCI group had ↓ BMD at the femoral neck (30%, $P < 0.0001$) and at the trochanter (39%, $P < 0.0001$) compared with AB controls. Also had ↓ BMC in lower limb (48%, $P < 0.0001$) and pelvis (55%, $P < 0.0001$). Blood phosphate level and urinary phosphate level were ↑ ($P < 0.01$) in group with SCI compared with AB controls. Urinary levels of calcium ($P < 0.001$), hydroxyproline ($P < 0.0001$), and deoxypiridoline ($P < 0.01$) are ↑ in group with SCI compared with AB controls.
Bauman *et al.*[66]; USA D & B = 10 *N* = 50 Cross-sectional with AB controls	100 men with SCI; mean age 51 ± 14 years; mean YPI 20 ± 13 (1–48 years). Comparison of serum calcium (Ca), phosphorus (PO4), albumin, alkaline phosphatase (Alk P), and PTH with serum 25-hydroxyvitamin D [25(OH)D] with AB controls (*n* =50), age and gender matched. Outcome measure: radioimmunoassay methods.	Approximately ⅓ of group with SCI were vitamin D deficient, which was a ↑ ($P = 0.05$) percentage than AB controls. Mean serum 25(OH) D was ↑ ($P < 0.0005$) in group with SCI compared to AB controls.
Slade *et al.*[59]; USA D & B = 11 *N* = 36 Cross-sectional with AB controls	19 women with complete SCI; mean age of premenopausal (< 30 years) 23.0 ± 2.55 years; mean YPI 5.6 ± 2.33 years, mean age of premenopausal (>35 years) 42.6 ± 4.66 years; mean YPI 12.2 ± 8.14 years; mean age of post-menopausal 54.5 ± 7.7 years; mean YPI 14.17 ± 11.9 years; Comparison of trabecular bone of the knee with AB controls (*n* =17), age and gender matched. Outcome measure: DEXA; magnetic resonance imager.	SCI group: trabecular bone was significantly ↓ compared with AB controls. SCI groups had fewer (−19 and −26% less) and thinner trabeculae (−6%) that were spaced further apart (40 and 62% more space between structures) resulting in less trabecular bone volume (−22 and −33%) compared with AB controls.
Amsters & Nitz[68] Australia D & B = 8 *N* = 60 Cross-sectional with AB controls	30 men with tetraplegia; four groups (age > 50 years and YPI< 5 years; age < 40 years & YPI < 5years; age > 50 years & YPI > 15 years; age < 40 years & YPI > 15 years). Comparison of posture with AB controls (*n* =30), age and gender matched. Outcome measure: photography of bony landmarks.	Group with SCI had ↑ thoracic kyphosis ($P < 0.05$) than AB controls. Regardless of age and duration of injury, persons with SCI do not sit with greater pelvic tilt than AB controls.
Lal[72]; USA D & B = 7 *N* = 53 Longitudinal	35 men and 18 women with SCI; mean age 37 (19–81 years) at baseline. Incidence of degenerative shoulder changes at baseline, and every two years until 5–15 YPI. Outcome measure: X-rays.	72% of sample demonstrated radiological evidence of degenerative changes, but only 11% reported shoulder pain. Persons with ↑ age (< 30 years) had ↑ incidence of radiographic changes. Premature shoulder changes appear primarily in wheelchair users of advanced age in less than 10 yrs with predilection of acromioclavicular joint.
Kivimaki & Ahoniemi[73]; Finland D & B = 23 *N* = 223 Cross-sectional with AB controls	96 men and 24 women with SCI; age range 18–65 years; mean age of group with paraplegia 47.0 ± 13.1, mean YPI 8.9 ± 12.0; mean age of group with tetraplegia 45.0 ± 14.8, mean YPI 6.7 ± 8.6. Comparison of shoulders with AB controls (*n* =103), age and gender matched. Outcome measure: ultrasonography.	Osteophytes were found in shoulders of 14% of AB controls, 22% in group with paraplegia, and 26% in group with tetraplegia ($P < 0.05$). Although no differences were found in the thickness of the supraspinatus tendon between groups, the mean thickness of bicipital tendon sheath was ↓ ($P < 0.01$) in AB controls compared to group with SCI. Wear and tear changes of the glenohumeral joint appear to be frequent in persons with SCI.
Pentland & Twomey[71] Australia D & B = 12 *N* = 104 Cross-sectional with AB controls	52 men with complete paraplegia; mean age 44 ± 12 years (2 groups: < 45 years; ≥ 45 years); mean YPI 17 ± 11 years (1 – 45 years). Comparison of bilateral upper limb physical functions with AB controls (*n* =52), age, gender, and activity matched. Outcome measure: concentric isokinetic average torque for shoulder; elbow flexion/extension; shoulder adduction and eccentric shoulder adduction; grip strength; shoulder and elbow active range of motion; upper limb pain.	AB controls had greater bilateral shoulder flexion than group with SCI, but group with SCI had greater bilateral elbow extension. Impairment and activity level were better predictors of strength in 9/14 muscles tested, whereas age was a better predictor in AB group.
Siddall *et al.*[70] Australia	60 men and 13 women with SCI; mean age at baseline 40 (21–81 years); mean YPI at baseline < 6 months.	Mean onset for musculoskeletal pain was at 1.3 ± 1.7 yrs, with a high prevalence at 5 yrs with an initial decline in the first 6 months post-injury.

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Article	Methods	Results
D & B = 18 *N* =73 Longitudinal	Assessed the prevalence, onset, and severity of pain at <1 YPI and at 5 YPI. Outcome measure: pain intensity via numeric scale; psychological distress; Von Korff chronic pain disability to assess pain interference on daily activities.	
Jensen *et al.*[69] USA D & B = 14 *N* = 147 Longitudinal	110 men and 37 women with SCI; mean age at follow-up 48.8 ± 13.0 (21–88 years); mean YPI at follow-up 16.6 ± 10.4 (3.2–57.4 years). Examined the change in the prevalence and intensity of pain over time (range 2–6 years between assessments). Outcome measure: brief pain inventory interference scale; bodily pain scale; SF-36; mental health scale.	The proportion of participants (34.7–48.3%) reporting shoulder pain ↑ ($P < 0.001$) over time.
Petrofsky & Laymon[35] USA D & B = 13 *N* = 100 Cross-sectional with AB controls	50 men with complete paraplegia; four age groups (20–30 years, 31–40 years, 41–50 years, 51–65 years); YPI range 3 – 10 years. Comparison of strength and endurance during isometric exercise and at rest (leg and arms) with AB controls, age, gender, and height matched. Outcome measure: dynamometer.	Group with SCI were stronger ($P < 0.05$) in handgrip strength than any of the AB controls in any age group examined. Knee strength was stronger ($P < 0.05$) in AB controls than in the SCI group. Both controls and SCI group showed a reduction of strength in their quadriceps associated with aging.

Abbreviations: AB, able-bodied; AP, anteroposterior; BMC, bone mineral content; BMD, bone mineral density; D and B, Downs & Black Score; DEXA, dual-energy X-ray absorptiometry; IALS, interpophysolaminar spaces; PQCT, peripheral quantitative computerized tomography; PTH, parathyroid hormone; SCI, spinal cord injury; SHBG, sex hormone-binding globulin; USBD, ultrasound bone densitometer; YPI, years post-injury.

Table 5

Respiratory system

Article	Methods	Results
Bach and Wang[74] USA D & B = 12 *N* = 10 Longitudinal	9 men and 1 woman with tetraplegia; mean age 41± 12.3 (34 – 77 years); mean YPI 7.7 ± 5.8 (6 months-19 years). Comparison of oxygen desaturation of SCI at baseline with 5-year follow up. Outcome measure: pulse oximetry.	At baseline, 6 subjects had desaturation below 90%. At follow-up, 5 subjects had an increased number of transient nocturnal oxygen desaturations.
Cahan *et al.*[75] Australia D & B = 12 *N* = 28 Cross-sectional with AB controls	16 men with tetraplegia; mean age 49 ± 15 (23–64 years); mean YPI 14 ± 10 (1–32 years). Comparison of oxygen desaturation with AB controls (*n* = 12), age and gender matched. Outcome measure: pulse oximetry.	6 patients with tetraplegia had ↓ in oxygen saturation levels below the normative range, indicative of SDB.
Biering-Sorensen and Biering-Sorensen[76] Denmark D & B = 16 *N* = 747 Cross-sectional with AB controls	331 men and 77 women; mean age 42.5 ± 14.1 (17–86 years); mean YPI 12.1 ± 6.3 (2.5 – 45.1 years). Comparison of oxygen desaturation with AB controls (*n* = 339) when awake and asleep, age and gender matched. Outcome measure: nordic sleep questionnaire.	Subjects with SCI snored more often ($P < 0.00001$), louder ($P = 0.013$), for more years ($P = 0.011$), and started at younger ages ($P < 0.00001$) compared with AB controls.
Loveridge *et al.*[77] Canada D & B = 11 *N* = 24 Cross-sectional with AB controls.	6 men with acute SCI; mean age 30 ± 11; for persons with tetraplegia; mean age 32.6 (21–50 years); mean YPI 38.6 months. Comparison of lung function and breathing patterns with AB controls (*n* = 18) in both sitting and supine positions, age and gender matched. Breathing function was assessed at 3, 6, and > 12 months post-injury. Outcome measure: lung function parameters including, force vital capacity, inspiratory capacity, residual volume, forced expiratory capacity, functional residual capacity, and maximum inspiratory mouth pressure; breathing pattern indicators including, Inspiratory time, tidal volume, and expiratory time.	Seating position resulted in greater stress on the respiratory system and breathing patterns in the group with tetraplegia compared with the AB control group. Over time, breathing patterns of the group with tetraplegia improved and were comparable to those of the AB control group.

Abbreviations: AB, able-bodied; D and B, Downs & Black Score; SCI, spinal cord injury; SDB, sleep disordered breathing; YPI, years post-injury.

Table 6

Skin and subcutaneous tissues

Article	Methods	Results
Rodriguez and Claus-Walker[78] USA D & B = 8 *N* = 15 Cross-sectional with AB controls	10 men with SCI; age range 14–50 years; YPI < 6 months. Comparison of skin degradation with AB controls (*n* = 5), age and gender matched. Outcome measure: glu-gal Hyl and gal Hyl from urine samples.	Although not statistically significant, the concentration of Glu-gal Hyl and gal Hyl were consistent, whereas the group with SCI had a very wide range of values.
Rodriguez and Garber[79] USA D & B = 15 *N* = 60 Longitudinal	60 men with SCI; with at least 1 past stage II pressure ulcer; age range 22–49 years; YPI < 1 year. Monitored changes in skin metabolism for 2 years in relation to pressure ulcer symptoms. Outcome measure: 24-h urine sample every 4–6 weeks used to determine concentrations of glu-gal Hyl, gal Hyl, calcium, and creatinine.	Subjects with sustained elevated concentration of glu-gal Hyl (more than 100 μmole/g creatinine) were significantly more likely to develop pressure ulcers. More smokers than non-smokers developed ulcers. The majority of persons who developed ulcers had injuries of T6 and above.

Abbreviations: AB, able-bodied; D and B, Downs & Black; SCI, spinal cord injury; YPI, years post-injury.

Table 7

Genitourinary and gastrointestinal systems

Article	Methods	Results
Scott *et al.*[86] USA D & B = 11 *N* = 22 530 Cross-sectional with AB controls	636 men with SCI; ages 50 +. Comparison of incidence and characteristics of prostate cancer with AB controls (*n* = 20 949) and men with prostate cancer (*n* = 945) Outcome measure: SCI, cancer registry, and outpatient databases.	1.7% of SCI group had been diagnosed with prostate cancer compared to 4.4% of AB controls. Average serum prostate specific antigen (PSA) level at diagnosis was significantly ↑ (*P* = 0.043) in group with SCI compared to AB controls. Group with SCI + prostate cancer (7; 63.6%) had locally advanced (stage T3) or metastactic prostate cancer (*P* = 0.012) compared to AB population (267; 29.1%).
Pramjudi *et al.*[89] USA D & B = 13 *N* = 737 Cross-sectional with AB controls	366 men with SCI; age range 40–79 (40–49 years, 50–59 years, 60–69 years, and 70–79 years). Comparison of serum PSA with age and gender matched AB controls (*n* = 371) Outcome measure: Abbott AxSym assay.	No differences in PSA levels between group with SCI and AB controls.
Konety *et al.*[85] USA D & B = 12 *N* = 79 Cross-sectional with AB controls	All men with SCI; age range 40–89 years (40–49 years, 50 – 59 years, 60–69 years, 70–79 years, and 80–89 years). Comparison of serum PSA with AB controls (*n* = 501), age and gender matched. Outcome measure: Abbot MEIA assay.	No differences in PSA levels between group with SCI and AB controls.
Shim *et al.*[90] Korea D & B = 12 *N* = 62 Cross-sectional with AB controls	31 men with SCI, median age 58 (45–81 years); median YPI 32 (5–55 years). Comparison of serum PSA with AB controls (*n* = 31), age and gender matched. Outcome measure: immunoradiometric assay; digital rectal examination; transrectal ultrasonography.	No differences in PSA levels and prostate volume parameters between group with SCI and AB controls.
Pannek *et al.*[87] Germany D & B = 10 *N* = 675 Cross-sectional with AB controls	100 men with SCI, mean age 53.7 ± 11.3 (35 –≥71 years). Comparison of prostate size and serum PSA with AB controls (*n* = 575), age and gender matched. Outcome measure: immunoenzymatic assay; transrectal ultrasonography.	No differences in prostate size or PSA levels between group with SCI and AB controls. Mean serum PSA level in the AB controls was found to ↑ with age, but shown to be of a lesser extent in persons with SCI.
Alexandrino *et al.*[88] Brazil D & B = 13 *N* = 88 Cross-sectional with AB controls	44 men with SCI, mean age 33.98 ± 9.12 (18–58 years). Comparison of total serum prostate specific antigen (PSA) and seminal PSA with AB controls (*n* = 44), age and gender matched. Outcome measure: Abbot AxSYM assay.	No differences in total PSA levels between group with SCI and AB controls. Total seminal PSA was ↓ (*P* = 0.0012) in group with SCI compared to AB controls.
Lamid *et al.*[83] USA D & B = 13 *N* = 32 Longitudinal	All men with SCI; mean age 29.72 (19 – 66 years) at injury. Medical chart review of annual visits from SCI patients with vesicoureteral reflux until 12 YPI. Outcome measures: medical records with information on bladder function, including radiological and laboratory examinations.	The majority of refluxes developed 1–2 YPI, and some disappeared spontaneously without causing damage to the urinary tract. After 4 YPI, the number of refluxes ↑ and progressed to grade II and IV, causing kidney damage with caliectasis.
Dewire *et al.*[80] USA D & B = 16 *N* = 57 Longitudinal	57 men with cervical SCI. Comparison of incidence of urological complications and renal deterioration in SCI patients with and without a chronic indwelling urinary catheter from baseline to 10 YPI. Outcome measure: patients' medical records excretory urogram.	No significant difference found between patients with and without chronic indwelling urinary catheters.

Article	Methods	Results
Sekar *et al.*[81] USA D & B = 16 *N* = 1 114 Longitudinal	915 men and 199 women with SCI; mean age 31.25 ± 13.79 (1–87 years) at injury. Evaluated the effects of different bladder management methods on long-term renal function for at least 10 YPI. Outcome measure: total and individual kidney ERPF.	A decreasing trend in mean ERPF was detected over time after injury, except for a slight reversal at 10 YPI.
Viera *et al.*[82] USA D & B = 15 *N* = 99 Longitudinal	77 men and 22 women; age range 14–65 years at injury. Investigated the effect of current bladder management techniques on renal function at 6–60 months post-injury. Outcome measure: serum creatinine, eExcretory urogram. Determination of short renal clearance ofiothalamate.	In the indwelling catheter group (*n* = 9), bladder calculi occurred in 3 patients at 7, 28, and 44 months post-injury, and were the only group to develop bladder stones. Excretory urogram abnormalities tended to occur earlier in the intermittent self-catheterization group (first 18 months) than in the bladder retraining group (third year).
Kuhlemeier *et al.*[84] USA D & B = 9 *N* = 687 Cross-sectional with AB controls	160 acute and 240 chronic; age range 16–60 years, YPI range for chronic 6–6 months. Comparison of renal function with AB controls, age and gender matched (*n* = 287). Outcome measure: computer-assisted renal scintigraphy.	Both individual and global kidney effective plasma flows were ↓ in the acute SCI group for persons who were 21–50 years old, but no difference existed for persons younger than 20 or older than 50.
Lynch *et al.*[95] New Zealand D & B = 16 *N* = 934 Cross-sectional with AB controls	384 men and 83 women with SCI; mean age 43.5 (15–89 years); mean YPI 14 (0.7–42.1 years). Comparison of bowel functioning with age and gender matched AB controls (*n* = 467). Outcome measure: mean fecal incontinence score, bowel motion frequency, haemorrhoidectomy, time at toilet, assistance at toilet.	SCI had ↑ fecal incontinence, less frequent bowel motion, spent longer times on the toilet, and required more assistance.
Krogh *et al.*[92] Denmark D & B = 16 *N* = 60 Cross-sectional with AB controls	11 men and 15 women; age range 17–69 years; YPI range 11–24 days. Comparison of total GITTs and segmental CTTs with age and gender matched AB controls (*n* = 24). Outcome measure: GITT and CTT.	GITT and CTT are significantly prolonged in SCI patients than in AB controls.
Menardo *et al.*[94] Italy D & B = 10 *N* = 48 Cross-sectional with AB controls	8 men and 3 women with SCI; age range 17–63 years YPI range 2 months 15 years. Comparison of transit of contents through the large bowel with AB controls (*n* = 37), age matched. Outcome measure: GITTs.	Compared with AB controls, GITT was ↓ in all patients with paraplegia. Flow contents through the left colon was markedly ↓ in group with SCI compared to AB controls, and transit of contents in 8 persons with SCI were ↓, and below the normal range of the AB controls.
Faaborg *et al.*[91] United Kingdom D & B = 12 *N* = 159 Longitudinal	114 men and 45 women with SCI; mean age at time 2: 37 (15–70 years); mean YPI at time 2: 10 (0–48 years). Assessed colorectal function over a 10-year period (1996 and 2006). Outcome measure: NBD score.	Constipation-related symptoms ↑ in the 10-year period ($P < 0.001$). The time needed for each defecation was > 30 min in 24 at time 1, and the corresponding number was 37 at time 2 ($P < 0.00001$). As well, the need for digital stimulation or evacuation of the anorectum every day or at least once per week ↑ from 34 and 69 to 48 ($P < 0.00005$) and 80 ($P < 0.00001$), respectively. Use of oral laxatives, suppositories and enema, and need for assistance did not ↑ between time periods. Persons reporting fecal incontinence at least once every month ↓ ($P < 0.001$) between time periods.
Emmanuel *et al.*[93] United Kingdom D & B = 9 *N* = 81 Cross-sectional with AB controls	45 men and 10 women with complete SCI; mean age 36 (19 – 68 years); mean YPI 34 months (13–134 months). Comparison of rectal muscosal blood flow with age matched AB controls (*n* = 26). Outcome measure: Doppler probe.	Compared with AB controls, resting blood flow was ↑ in persons with lesions above T5 ($P = 0.056$) and similar in persons with lesions below T5. Compared with AB controls, 6 patients with lesions below T5 had a tendency towards a ↓in mucosal blood flow, although this was not significant.

Abbreviations: AB, able-bodied; CTT, colorectal transit time; D and B, Downs and Black score; ERPF, effective renal plasma flow; GITT, gastrointestinal transit times; NBD, neurogenic bowel dysfunction; PSA, prostate-specific antigen; SCI, spinal cord injury; YPI, years post-injury.

Table 8

Nervous system

Article	Methods	Results
Siddall *et al.*[70] Australia D & B = 18 *N* = 73 Longitudinal	60 men and 13 women with SCI; mean age at baseline 40 (21–81 years); mean YPI at baseline < 6 months. Assessed the prevalence, onset, and severity of pain at < 1 YPI and at 5 YPI. Outcome measure: pain intensity via numeric scale; psychological distress; Von Korff chronic pain disability to assess pain interference on daily activities.	Persons with neuropathic pain early following injury were likely to continue to experience ongoing and severe pain.
Putzke *et al.*[96] USA D & B = 17 *N* = 270 Longitudinal	210 men and 60 women with SCI; mean age at 1 YPI 36.8 ± 14.3 years. Examined factors that contribute to pain interference at 1 and 2 YPI. Outcome measure: short-form 12.	Age effect for pain interference was detected ($P < 0.001$). Youngest group with SCI who reported no pain interference at both year 1 and year 2, and the oldest group being those reporting pain interference at both year 1 and year 2.
Rintala *et al.*[97] USA D & B = 18 *N* = 96 Longitudinal	69 men and 27 women with SCI; phase I: male mean age 40.5 ± 12.5 (23–70 years); mean YPI 11.1 ± 8.8; female mean age 37.0 ± 10.8 (21–61 years); mean YPI 10.4 ± 7.2 years). Assessed the consistency of pain at three (women) and four (men) measurement points across 10 years. Outcome measure: self-report pain characteristics.	Of the 96 participants, approximately half the men and three-quarters of women reported consistent pain across all measurement points.
Jensen *et al.*[69] USA D & B = 14 *N* = 147 Longitudinal	110 men and 37 women with SCI; mean age at follow-up 48.8 ± 13.0 (21–88 years); mean YPI at follow-up 16.6 ± 10.4 (3.2–57.4 years). Examine the change in the prevalence and intensity of pain over time (range 2–6 years between assessments). Outcome measure: brief pain inventory interference scale; bodily pain scale; SF-36; mental health scale.	Overall, the change or intensity in the prevalence of pain over time was not significant.

Abbreviations: AB, able-bodied; D and B, Downs & Black Score; YPI, years post-injury.