**Authors:**

Angela M. Garcia, MD
Brad E. Dicianno, MD

**Affiliations:**

From the Dept. of Physical Medicine and Rehabilitation (AMG, BED); Adult Outpatient Spina Bifida Clinic University of Pittsburgh Medical Center (UPMC) (BED); Human Engineering Research Laboratories, VA Pittsburgh Healthcare System (BED); and Dept. of Rehabilitation Science and Technology, University of Pittsburgh (BED), Pennsylvania.

**Correspondence:**

All correspondence and requests for reprints should be addressed to: Brad E. Dicianno, MD, UPMC Dept. of Physical Medicine and Rehabilitation, 3471 5th Avenue, Suite 202, Pittsburgh, PA 15213.

**Disclosures:**

Funded by the UPMC Department of Physical Medicine and Rehabilitation. Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.

0894-9115/11/9002-0089/0
*American Journal of Physical Medicine & Rehabilitation*


DOI: 10.1097/PHM.0b013e318201753e



ORIGINAL RESEARCH ARTICLE

# The Frequency of Lymphedema in an Adult Spina Bifida Population

## ABSTRACT

Garcia AM, Dicianno BE: The frequency of lymphedema in an adult spina bifida population. Am J Phys Med Rehabil 2011;90:89–96.

**Objective:** In the United States, there are more than 100,000 people with spina bifida. There have been very few studies to date documenting the occurrence of lymphedema in the spina bifida population, despite a case series in 2001 that suggested that the occurrence may be higher than in the general population. Currently, approximately 1 million people have lymphedema in the United States. The purpose of this study was to document the occurrence of lymphedema and associated medical factors in a regional adult spina bifida population.

**Design:** A total of 240 electronic medical records from the Adult Spina Bifida Clinic from January 2005 to August 2008 were retrospectively reviewed. Subjects were divided into two groups based on the presence or absence of lymphedema. $\chi^2$ analyses were used to compare lymphedema groups with respect to history of medical comorbidities and ethnicity. Fisher exact tests were used to compare groups with respect to mobility status and the presence of power wheelchair seat functions. Mann-Whitney U tests were used to compare groups with respect to age, anatomic lesion level, employment level, and income.

**Results:** Twenty-two (9.2%) patients had lymphedema. Mean ± SD population age was 35.1 ± 11.1 yrs. Lymphedema was associated with a history of trauma ($P = 0.044$), cellulitis ($P < 0.001$), cancer ($P = 0.038$), obesity ($P < 0.001$), wounds ($P < 0.001$), hypertension ($P = 0.036$), higher lesion level spina bifida ($P = 0.049$), and mobility status ($P = 0.007$). Hypertension and obesity were present in 38.3% and 37.5% of the total study population, respectively.

**Conclusions:** This is the first study to document the occurrence of lymphedema in a spina bifida patient population, which was almost 100 times higher than that in the general patient population. We also documented a high occurrence of hypertension and obesity in the total study population. These findings may help guide further prospective studies to more clearly delineate the risk factors for the development of lymphedema and to determine the appropriate therapies. Better screening, prevention and treatment algorithms are needed for hypertension and obesity in the spina bifida population.

**Key Words:** Meningomyelocele, Lymphedema, Hypertension, Obesity

Spina bifida (SB), which is the result of failure of closure of the neural tube in embryonic development, is one of the most common congenital malformations seen worldwide. In the United States, SB occurs in approximately 1.90 of every 10,000 live births,[1] with now more than 100,000 people living with SB.[2] As many as 85%–90% of individuals with SB are now surviving into adulthood because of advancements in medical and surgical care and thus live with many chronic, disabling medical comorbidities.[3] We reported in a recent comprehensive review of medical literature on adult SB[4] that there have not been any randomized controlled studies, prospective cohort studies, or retrospective cohort studies to date on lymphedema in this population, despite the fact that a case series by Rockson et al.[5] suggested that the occurrence rate in the SB population may be much higher than that in the general population.

Lymphedema is a chronic, edematous state resulting from dysfunction of lymphatic transport, which allows for the buildup of protein and fluid in the interstitium.[6] The lymphatic system consists of the lymphatic vessels and tissues and has several functions, including tissue-fluid homeostasis, immune surveillance, and absorption of triglycerides and chylomicrons in the intestines.[7,8] The lymphatic system returns protein, water, fatty acids, salts, microorganisms, foreign debris, lymphocytes, and antigen-presenting cells from the interstitial tissues to the blood circulation.[8,9] These fluids and molecules are continuously filtering into the interstitial tissues secondary to the blood pressure within the arterial capillaries. Ninety percent of these are reabsorbed by the venous capillaries (secondary to increased colloid osmotic pressure that exceeds the blood pressure), and this 10% is reabsorbed via the lymphatic vasculature.[10,11]

The lymphatic system is made up of highly permeable lymphatic capillary vessels, made up of a single layer of lymphatic epithelial cells. The cells are not surrounded by pericytes or smooth muscle cells. The lymphatic cells have little or no basement membrane and discontinuous interendothelial junctions.[10,12,13] Lymphatic capillaries are located in the tissues and are connected to the extracellular matrix and collagen via anchoring filaments. The anchoring filaments become taut in times of tissue edema and open the vessel lumen. This decreases the intraluminal pressure, allowing fluid to flow into the capillary. The lymph is then moved into precollector vessels, which are surrounded by a sparse layer of smooth muscle.[12–14] Precollector vessels then join and fuse to form the lymphatic vessels. These are characterized by the presence of a smooth muscle layer, basement membrane, continuous interendothelial junctions, and bileaflet valves.[10,12,13] Lymph is propelled forward by the action of the smooth muscle layer, along with the contraction of the skeletal muscles surrounding the vessels, and arterial pulsations.[10,15] Lymphatic vessels all drain into two structures, the thoracic duct to the left subclavian vein or the right lymphatic trunk to the right subclavian vein. In a properly functioning lymphatic system, the lymphatic vasculature will return approximately 1–2 liters of interstitial fluid and 20–30 g of protein to the venous system daily.[10,16]

There are approximately 1 million people with lymphedema in the United States, affecting 0.1% of the population.[17,18] Lymphedema is categorized as either primary or secondary.[6,9] Primary lymphedema is a congenital abnormality of the lymphatic system, whereas secondary lymphedema involves an obstruction of a normal lymphatic system resulting from a disease or medical process.[6,9] Congenital abnormalities can range from hypoplasia (reduced lymphatic vessels or reduced diameter of lymphatic vessels) to hyperplasia (increased number of lymphatic vessels) to aplasia (absence of lymphatic vessels) to fibrosis of the inguinal lymph nodes.[9] Reported risk factors for the development of secondary lymphedema in the general population include previous surgical procedures, history of radiation therapy, trauma, infection, travel to an area of endemic filariasis, malignancy, or obesity.[6,9] Associated complications of lymphedema include recurrent cellulitis, chronic skin breakdown, hyperkeratosis, and development of cutaneous malignant tumors.[6] Lymphedema has been associated with greater levels of functional impairment, depression, social isolation, and a decrease in quality-of-life.[19,20] The aims of this study were to be the first to estimate the occurrence of lymphedema in the SB population and to identify the possible factors related to the presence of lymphedema.

## METHODS

Data were collected in an unidentifiable manner; therefore, this study is exempt from institutional review board review, as confirmed by the institutional review board at the University of Pittsburgh. Data collection was completed through a retrospective chart review using an electronic medical record system of 240 patients seen in a university-based adult SB clinic from January 2005 to August 2008.

Inclusion criteria were a clinical diagnosis of SB cystica and age greater than 18 yrs. Charts from individuals with a history of SB occulta were excluded. We recorded the presence or absence of lymphedema and the anatomical level of the spinal lesion as determined by a physiatrist based on the patient's charted history and physical examination findings (muscle strength testing and sensory testing). Several medical comorbidities that have been previously identified as potential risk factors for lymphedema (chronic venous insufficiency, trauma, history of radiation therapy, hypertension, cancer, cellulitis, infection, and wounds) identified in the medical history of the patients were also recorded.[6,9,21] Each patient was examined by a single physician. This allowed for standardized assessment and documentation as to the presence or absence of lymphedema and other comorbid medical conditions. The diagnosis of lymphedema was determined by the presence of nonpitting edema that does not resolve with leg elevation, positive Stemmer sign, or by having a previous diagnosis of lymphedema in the electronic medical record. Patients who reported having a history of cancer were routinely asked about the type of treatments that they received, including radiation therapy. Hypertension was defined as having a systolic blood pressure greater than 140 mm Hg, per the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines[22]; taking a blood pressure medication; or having a listed medical history of hypertension. Obesity was defined as having a body mass index greater than 30 kg/m$^2$ based on their weight and self-reported height recorded during a clinic visit. Descriptive demographic information, including age, sex, ethnicity, employment status, income, and mobility status (categorized as ambulators, manual wheelchair users, or power mobility based on the individual's self-reported primary method of mobility), was collected. If an individual used power mobility, information was taken on what

**TABLE 1** Demographic variables of a university-associated adult spina bifida clinic with and without lymphedema

| | Individuals Without Lymphedema ($n = 218$) | | Individuals with Lymphedema ($n = 22$) | | |
|---|---|---|---|---|---|
| | *n* | % | *n* | % | *P* |
| Age, mean ± SD, yrs | 35.3 ± 11.4 | | 33.7 ± 7.2 | | 0.960[a] |
| Sex | | | | | 0.237[b] |
| Females | 120 | 55.05 | 15 | 68.18 | |
| Males | 98 | 44.95 | 7 | 31.82 | |
| Ethnicity | | | | | 0.836[b] |
| Caucasian | 177 | 81.19 | 17 | 77.27 | |
| African American | 3 | 1.38 | 2 | 9.09 | |
| Asian American | 12 | 5.50 | 2 | 9.09 | |
| Hispanic | 1 | 0.46 | 0 | 0.0 | |
| Multiracial | 4 | 1.83 | 0 | 0.0 | |
| Other | 2 | 0.92 | 0 | 0.0 | |
| Unknown | 19 | 8.72 | 1 | 4.55 | |
| Employment status | | | | | 0.746[a] |
| Unemployed | 126 | 57.80 | 13 | 59.09 | |
| Part-time | 55 | 25.23 | 7 | 31.82 | |
| Full-time | 35 | 16.06 | 1 | 4.55 | |
| Unknown | 2 | 0.92 | 1 | 4.55 | |
| Income (yearly) | | | | | 0.558[a] |
| <10,000 | 63 | 28.90 | 10 | 45.45 | |
| 10,000–15,000 | 18 | 8.26 | 2 | 9.09 | |
| 15,001–20,000 | 13 | 5.96 | 0 | 0.00 | |
| 20,001–25,000 | 14 | 6.42 | 1 | 4.55 | |
| 25,001–35,000 | 17 | 7.80 | 0 | 0.00 | |
| 35,001–50,000 | 17 | 7.80 | 1 | 4.55 | |
| 50,001–75,000 | 18 | 8.26 | 1 | 4.55 | |
| >75,000 | 15 | 6.88 | 0 | 0.00 | |
| Unknown | 43 | 19.72 | 7 | 31.82 | |

[a]Mann-Whitney *U* statistical analysis.
[b]$\chi^2$ statistical analysis.

**TABLE 2** Association between the spina bifida anatomic lesion level and the frequency of lymphedema

| | Individuals Without Lymphedema ($n$ = 218) | | Individuals with Lymphedema ($n$ = 22) | | |
|---|---|---|---|---|---|
| Lesion Level | $n$ | % | $n$ | % | $P$[a] |
| Sacral | 11 | 5.05 | 1 | 4.55 | 0.049[a] |
| Lumbar | 155 | 71.10 | 13 | 59.09 | |
| Thoracic | 43 | 19.72 | 8 | 36.36 | |
| Sacral agenesis | 6 | 2.75 | 0 | 0.00 | |
| Not documented | 3 | 1.38 | 0 | 0.00 | |

[a]Mann-Whitney $U$ statistical analysis.

power seat functions were available on the power wheelchair (power elevating leg rests, tilt-in-space, and recline).

Subjects were divided into two groups: those with no history of lymphedema (lymphedema (−) group) and those with a history of lymphedema (lymphedema (+) group). Statistical analyses were completed using SPSS version 16.0. The total number of comorbid conditions for each subject was summed. $\chi^2$ analyses were used to compare lymphedema groups with respect to history of each medical comorbidity, sex, and ethnicity. Monte Carlo and Fisher exact statistics were used to compare groups with respect to mobility status and the presence of power wheelchair seat functions, respectively. Mann-Whitney $U$ tests were used to compare groups with respect to number of comorbid conditions, age, lesion level, employment level, and income. Level of significance was set as $P < 0.05$.

## RESULTS

A total of 240 medical records were reviewed. There were 218 (90.8%) individuals (mean ± SD age, 35.3 ± 11.4 yrs) who did not carry a diagnosis of lymphedema and 22 (9.2%) individuals (mean ± SD age, 33.7 ± 7.2 yrs) who carried a diagnosis of lymphedema. Of the individuals with lymphedema, 1 (4.5%) had unilateral involvement of the lower limbs, whereas 21 (95.5%) had bilateral involvement of the lower limbs. There were no cases of upper limb lymphedema. Table 1 shows the demographic information for both groups (age, race, employment status, and income level for each group). There were no significant differences in age, sex, ethnicity, employment, or income between the two groups.

The lymphedema groups were significantly different with respect to anatomical lesion level (Table 2). The lymphedema (+) group had a greater percentage of individuals with a thoracic level lesion

**TABLE 3** Association between mobility status and the frequency of lymphedema in an adult spina bifida population

| | Individuals Without Lymphedema ($n$ = 218) | | Individuals with Lymphedema ($n$ = 22) | | |
|---|---|---|---|---|---|
| | $n$ | % | $n$ | % | $P$ |
| Mobility status[a] | | | | | 0.007[b] |
| Ambulators | 81 | 37.16 | 2 | 9.09 | |
| Manual wheelchairs | 98 | 44.95 | 12 | 54.55 | |
| Power | 38 | 17.43 | 8 | 36.36 | |
| Missing | 1 | 0.46 | 0 | 0.00 | |
| Power wheelchair features[a] | ($n$ = 38) | | ($n$ = 8) | | |
| Power leg rests | 18 | 47.37 | 5 | 62.50 | 0.35[c] |
| Tilt | 20 | 52.63 | 5 | 62.50 | 0.456[c] |
| Recline | 16 | 42.11 | 4 | 50.00 | 0.489[c] |

[a]Percentages do not add up to 100% because individuals may have reported the presence of more than one power mobility feature.

[b]Monte Carlo statistical analysis.

[c]Fisher exact test statistical analysis.

**TABLE 4** Association between the frequency of lymphedema and other comorbid medical diagnoses in an adult spina bifida population

| | Individuals Without Lymphedema ($n$ = 218) | | Individuals with Lymphedema ($n$ = 22) | | | |
|---|---|---|---|---|---|---|
| | $n$ | %[a] | $n$ | %[a] | $P$ | Odds Ratio |
| Medical condition | | | | | | |
| Chronic venous insufficiency | 20 | 0.09 | 3 | 0.14 | 0.498[b] | 1.56 |
| Trauma | 1 | 0.00 | 1 | 0.05 | 0.044[b] | 10.33 |
| Cellulitis | 1 | 0.00 | 5 | 0.23 | <0.001[b] | 63.80 |
| Cancer | 4 | 0.02 | 2 | 0.09 | 0.038[b] | 5.35 |
| Radiation therapy | 0 | 0.00 | 0 | 0.00 | 1.000[b] | [c] |
| Obese | 74 | 0.34 | 16 | 0.73 | <0.001[b] | 5.19 |
| Wound | 19 | 0.09 | 14 | 0.64 | <0.001[b] | 18.32 |
| Hypertension | 79 | 0.36 | 13 | 0.59 | 0.036[b] | 2.54 |
| No. medical conditions | | | | | <0.0001[d] | |
| 0 | 86 | 39.40 | 2 | 9.10 | | |
| 1 | 76 | 34.90 | 3 | 13.60 | | |
| 2 | 44 | 20.20 | 5 | 22.70 | | |
| 3 | 10 | 4.60 | 7 | 31.80 | | |
| 4 | 1 | 0.50 | 5 | 22.70 | | |
| Missing | 1 | 0.50 | 0 | 0.00 | | |

[a]Percentages do not add up to 100 because an individual may have had a history of several of the medical diagnoses listed.
[b]$\chi^2$ statistical analysis.
[c]Odds ratio was not calculated secondary to not having any patients who had radiation therapy in our study population.
[d]Mann-Whitney $U$ analysis.

than did the lymphedema (−) group. In addition, there was only 1 (4%) individual in the lymphedema (+) group with a sacral level lesion, compared with the lymphedema (−) group, which had 17 (8%) individuals with a sacral level lesion.

Table 3 shows the mobility status of each group. Lymphedema groups were significantly different with respect to mobility level. In the lymphedema (+) group, a greater percentage of individuals used power mobility (36.4%) compared with the lymphedema (−) group (only 17.4%). For those who used power wheelchairs, there were no differences between lymphedema groups with respect to the presence of power seat functions (elevating leg rests, tilt-in-space, or recline).

Table 4 shows the medical comorbidities associated with lymphedema in each of the groups. Lymphedema was significantly associated with history of trauma ($P$ = 0.044), cellulitis ($P$ < 0.001), wounds ($P$ < 0.001), cancer ($P$ = 0.038), obesity ($P$ < 0.001), and hypertension ($P$ < 0.001). Lymphedema was not associated with chronic venous insufficiency. No patients had a history of radiation therapy. Odds ratios were calculated, and overall, individuals with lymphedema had greater odds of having an association with each comorbid medical condition, except a history of radiation therapy. They were 63.8 times more likely to have an association with cellulitis compared with individuals without lymphedema. Overall, 90 (37.5%) individuals were identified as obese, and 92 (38.3%) individuals were identified as having hypertension.

## DISCUSSION

This is the first study of a large cohort of individuals to document the frequency of lymphedema in the adult SB population. The surprisingly high frequency rate of 9% is almost a 100-fold increase compared with the rate in the general population.[17,18] Reasons for this increase are unclear and should be targets of future research.

Potential associated factors for lymphedema in the general population include trauma, wounds, and cellulitis.[6,17] These problems could be part of a cyclical process where loss of skin integrity and infection puts an individual at risk for lymphedema, but the presence of lymphedema itself could be a risk factor for further breakdown and infection. Patients with SB are at increased risk of untreated limb trauma secondary to decreased sensation in the distribution of the affected spinal nerve roots. One of our recent studies[23] found that more than 10% of hospitalizations of individuals with SB were secondary to wounds or subcutaneous infections.

Inefficient muscular contraction secondary to muscle paresis could also predispose an individual to lymphedema. Muscle contraction does assist with lymphatic drainage and lymph fluid movement. Impairment of that contraction could lead to the backup of lymph within the vessels, increasing intravascular pressure, which makes it difficult for fluid to drain into the lymphatic capillaries.[10] Owing to the fact that other disabilities such as spinal cord injury do not have such a high occurrence rate of lymphedema, other factors such as either a developmental abnormality of the lymphatic system or chronic obstruction to lymphatic flow secondary to excessive pressures from dependent limbs or improper wheelchair fitting over an entire lifetime could be other potential causes. The association of lymphedema with higher lesion level and lower mobility status lends further evidence that those who use wheelchairs are at increased risk. Supporting this is the clinical observation that lymphedema does not seem to be common in the pediatric population, leading to a suspicion that a length-time relationship between wheelchair use and development of lymphedema may exist. However, this has not been studied within the pediatric or adult SB populations.

Increased tissue pressure caused by hypertension and obesity (together or alone) could collapse the vessels of the lymphatic vasculature, causing trapping of fluid in interstitial tissues, leading to lymphedema. A review[24] of skin manifestations associated with obesity in 2007 stated that obesity impedes lymphatic flow, which can lead to the collection of protein-rich fluid in the subcutaneous tissue, which will frequently result in lymphedema. A recent study by Helyer et al.[25] showed that obesity may be a risk factor for the development of lymphedema in breast cancer patients.[24] Hypertension itself has been associated with the development of lymphedema in cancer patients, but the mechanism is unknown.[9,21]

The same power seat functions were present on power wheelchairs, regardless of whether the users had lymphedema. Although it is known that dependent edema is treatable with a combination of tilt and recline, which can elevate the legs above the heart,[26] more research is needed to determine whether there is a similar effect for lymphedema. We retrospectively analyzed the relationship between chronic venous insufficiency and presence of power seat functions and also found no relationship in this group. Power seat functions may be prescribed for reasons other than edema, such as for positioning, pressure relief, or orthopedic purposes. One previous study showed that most people using power seat functions do not use them as prescribed.[27] Better patient education on how to manage edema with power seat functions may be necessary.

Interesting findings in this study included the overall occurrences of hypertension and obesity in this adult SB clinic population, which were 38.3% and 37.5%, respectively. Recent reviews of medical comorbidities of adult patients with SB by Webb[28] and Dicianno et al.[4] have noted the lack of studies expressing the occurrence of hypertension in the SB patient population. This study is the largest to date to look at the occurrence of hypertension in the adult SB population. These findings are similar to those found by Buffart et al.[29] in 2008, which reported an occurrence of hypertension in 20% of their study population ($n = 51$) in the Netherlands, and by Long and Green[30] in 2009, who found that 40% of their study population ($n = 42$) in the United Kingdom had hypertension. Hypertension in this population may be secondary to factors not explored here, including the presence of renal disease, obstructive sleep apnea, sedentary lifestyle, and nutrition. In addition, obesity also may be a predisposing factor, as it may cause microvascular dysfunction with the cutaneous tissues.[24]

The high occurrence rate of obesity in this adult SB clinic population is a concern as well. The finding that 37.5% of individuals at this adult SB clinic are obese is similar to other studies, which have found obesity rates in adolescents and adults to range from 35% to 37%.[29,31] Risk factors, which were not explored here, are numerous in this patient population, including a nonambulatory status, low activity levels, low lean muscle mass, and neuroendocrine abnormalities from hydrocephalus.[32,33]

## Limitations

Significant associations were found between lymphedema and anatomic lesion level, wheelchair use, and several medical comorbidities. However, it is likely that complex interactions exist among these variables that cannot be accounted for secondary to the retrospective study design. A higher level of lesion is associated with a higher degree of functional impairment,[4] which may result in wheelchair use or more complex medical problems. Certainly, additional prospective studies are warranted to further delineate causality and colinearity of the variables. History of hydrocephalus may also be negatively associated with functional status but was not examined here. Despite being cross-sectional and retrospective

in nature, this was the first study to document the occurrence rate of lymphedema in the SB population and serves as a way to identify potential associated factors that can be examined in larger studies.

The ethnic distribution of the subjects in our study was reflective of that in our geographic area but included a low number of individuals of Hispanic descent. Those of Hispanic descent have been shown to have a similar or greater incidence of SB than non-Hispanic Caucasians.[1,34] The occurrence of lymphedema in individuals of Hispanic descent has been mostly undocumented, with only one study in 2005[35] showing that Hispanic and African American women were significantly more likely to develop lymphedema after breast cancer treatment. Thus, this study has limited external validity to certain ethnic groups.

In addition, because of the small total number of patients with lymphedema ($n$ = 22) in the study population, the power to make associations is limited. This can be addressed in future research by using a multicenter, prospective study design. Although screening protocols for lymphedema were not addressed in this study, the associations found in this study could be used to help develop and test screening protocols in the future.

In addition, the treatment of lymphedema in this population was not explored at this time. Therefore, we are not able to comment on the availability of therapeutic options for the treatment of lymphedema or on their effectiveness. However, in this study population, any individual who is diagnosed with lymphedema through the adult SB clinic is referred to a physical therapist specializing in lymphedema therapy for further treatment.

## CONCLUSIONS

This is the first study to document the frequency of lymphedema in an adult SB population, which was found to be approximately 9%. This is almost 100 times higher than that in the general population. Physicians should be attuned to the possibility of this diagnosis in those with acute or chronic lower limb edema. In addition, the high occurrence rates of hypertension and obesity within this patient population may warrant better screening, prevention, and treatment options. Further multicenter orientated research is needed to determine the prevalence of lymphedema in the national adult SB population. Further research is also needed to determine the optimal screening and treatment protocols and to explore ways to prevent lymphedema in this patient population.

## REFERENCES


1. CfDCaP (CDC). Racial/ethnic differences in the birth prevalence of spina bifida—United States, 1995–2005. *MMWR Morb Mortal Wkly Rep* 2009;57:1409–13
2. Association SB. About Spina Bifida. Available at: http://www.spinabifidaassociation.org/site/c.liKWL7PLLrF/b.2642339/k.61F3/Living_With_Spina_Bifida.htm. Accessed May 24, 2010
3. Mukherjee S: Transition to adulthood in spina bifida: changing roles and expectations. *Sci World J* 2007;7:1890–5
4. Dicianno B, Kurowski B, Yang J, et al: Rehabilitation and medical management of the adult with spina bifida. *Am J Phys Med Rehabil* 2008;87:1027–50
5. Rockson SG, Bahreman A, Szuba A: Lymphedema in spina bifida: a case series. *Int J Angiol* 2001;9:188–90
6. Warren A, Brorson H, Borud L, Slavin S: Lymphedema: a comprehensive review. *Ann Plast Surg* 2007;59:464–72
7. Karpanen T, Alitalo K: Molecular biology and pathology of lymphangiogenesis. *Annu Rev Pathol* 2008;3:367–97
8. Bruyère F, Noël A: Lymphangiogenesis: in vitro and in vivo models. *FASEB J* 2010;24:8–21
9. Lawenda B, Mondry T, Johnstone P: Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. *CA Cancer J Clin* 2009;59:8–24
10. Tammela T, Alitalo K: Lymphangiogenesis: molecular mechanisms and future promise. *Cell* 2010;140:460–76
11. Földi M, Strössenreuther R: eds. *Foundations of Manual Lymph Drainage*. ed 3. New York, NY: Elsevier; 2004
12. Alitalo K, Tammela T, Petrova T: Lymphangiogenesis in development and human disease. *Nature* 2005;438:946–53
13. Baluk P, Fuxe J, Hashizume H, et al: Functionally specialized junctions between endothelial cells of lymphatic vessels. *J Exp Med* 2007;204:2349–62
14. Maby-El Hajjami H, Petrova T: Developmental and pathological lymphangiogenesis: from models to human disease. *Histochem Cell Biol* 2008;130:1063–78
15. Bazigou E, Xie S, Chen C, et al: Integrin-alpha9 is required for fibronectin matrix assembly during lymphatic valve morphogenesis. *Dev Cell* 2009;17:175–86
16. Levick JR: Changing perspective on microvascular fluid exchange. In Jordan D, Marshall J (eds): Cardiovascular Regulation. London, Portland Press, 1995, pp 127–52
17. *Medifocus Guidebook on Lymphedema: A Comprehensive Guide to Symptoms, Treatment, Research, and Support*. Silver Springs, MD: Medifocus.com, Inc; 2010:23–4

18. TW R: Lymphedema. *Keeping in Circulation: The Official Newsletter of the Vascular Disease Foundation*. 2006:1–2

19. Morgan P, Franks P, Moffatt C: Health-related quality of life with lymphoedema: a review of the literature. *Int Wound J* 2005;2:47–62

20. Person B, Addiss D, Bartholomew L, et al: "Can it be that God does not remember me": a qualitative study on the psychological distress, suffering, and coping of Dominican women with chronic filarial lymphedema and elephantiasis of the leg. *Health Care Women Int* 2008;29:349–65

21. Meek A: Breast radiotherapy and lymphedema. *Cancer* 1998;83:2788–97

22. Chobanian A, Bakris G, Black H, et al: The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003;289: 2560–72

23. Dicianno B, Wilson R: Hospitalizations of adults with spina bifida and congenital spinal cord anomalies. *Arch Phys Med Rehabil* 2010;91:529–35

24. Yosipovitch G, DeVore A, Dawn A: Obesity and the skin: skin physiology and skin manifestations of obesity. *J Am Acad Dermatol* 2007;56:901–16; quiz 17–20

25. Helyer L, Varnic M, Le L, Leong W, McCready D: Obesity is a risk factor for developing postoperative lymphedema in breast cancer patients. *Breast J* 2010; 16:48–54

26. Dicianno B, Arva J, Lieberman J, et al: RESNA position on the application of tilt, recline, and elevating legrests for wheelchairs. *Assist Technol* 2009;21: 13–22; quiz 4

27. Lacoste M, Weiss-Lambrou R, Allard M, Dansereau J: Powered tilt/recline systems: why and how are they used? *Assist Technol* 2003;15:58–68

28. Webb T: Optimizing health care for adults with spina bifida. *Dev Disabil Res Rev* 2010;16:76–81

29. Buffart L, van den Berg-Emons R, Burdorf A, Janssen W, Stam H, Roebroeck M: Cardiovascular disease risk factors and the relationships with physical activity, aerobic fitness, and body fat in adolescents and young adults with myelomeningocele. *Arch Phys Med Rehabil* 2008;89:2167–73

30. Long G, Green J: Journey into the unknown: a survey into the effects of ageing on the health of people with spina bifida and/or hydrocephalus in the West Midlands area. *Cerebrospinal Fluid Res* 2009;6:S29

31. Dosa N, Foley J, Eckrich M, Woodall-Ruff D, Liptak G: Obesity across the lifespan among persons with spina bifida. *Disabil Rehabil* 2009;31:914–20

32. Roebroeck M, Jahnsen R, Carona C, Kent R, Chamberlain M: Adult outcomes and lifespan issues for people with childhood-onset physical disability. *Dev Med Child Neurol* 2009;51:670–8

33. van den Berg-Emons H, Bussmann J, Meyerink H, Roebroeck M, Stam H: Body fat, fitness and level of everyday physical activity in adolescents and young adults with meningomyelocele. *J Rehabil Med* 2003; 35:271–5

34. Canfield M, Ramadhani T, Shaw G, et al: Anencephaly and spina bifida among Hispanics: maternal, sociodemographic, and acculturation factors in the National Birth Defects Prevention Study. *Birth Defects Res A Clin Mol Teratol* 2009;85:637–46

35. Eversley R, Estrin D, Dibble S, Wardlaw L, Pedrosa M, Favila-Penney W: Post-treatment symptoms among ethnic minority breast cancer survivors. *Oncol Nurs Forum* 2005;32:250–6