Original Clinical Article

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What influences contracture formation in lower motor neuron disorders, severity of denervation or residual muscle function? An analysis of the elbow contracture in 100 children with unilateral Brachial Plexus Birth Injury

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Abstract

Purpose As in other neuromuscular disorders, both denervation and muscle paresis/imbalance are implicated as aetiological factors for contractures in children with a Brachial Plexus Birth Injury (BPBI). Although both factors are related, it is unclear which factor is dominant. The aim of this study is to assess whether contracture formation in children is predominantly related to denervation or to residual muscle function/imbalance. This might be relevant for understanding contracture formation in other neuromuscular disorders.

Methods A total of 100 children (61 boys; mean age 10.4 years, 4 to 18) with unilateral BPBI were included in this cross-sectional study. Severity of the denervation was classified according to Narakas. Muscle function of flexors and extensors of both elbows was measured (in Newtons) using a hand-held dynamometer and flexion contractures were measured with a goniometer. The relation between denervation, muscle function/muscle balance and flexion contracture was assessed using univariate and multivariate analysis.

Results Of the children, 57 were Narakas class I, 13 class II and 30 class III. Mean flexion contracture was 25° (90° to -5°). At the affected side the forearm flexion force was 47% and extension force was 67% of the force of the unaffected side. Contractures were more severe in children with higher Narakas classifications (p = 0.001), after neurosurgery (Mann-Whitney U test, p = 0.009) and were related to age (Spearman's Rho = -0.3, p = 0.008) and to paresis of the extensors (Rho = 0.4, p = 0.000). Flexor paresis as a percentage of unaffected side (Rho = 0.06, p = 0.6) and muscle balance had no influence.

Conclusion In BPBI, elbow contractures are related to the severity of the neurological lesion, not to residual muscle function.

Level of evidence Level II – prognostic study

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Introduction

Joint and muscle contractures often occur in upper and in lower motor neuron disorders[1] and this relation between muscles, joint contractures and bone deformities has intrigued the profession for more than a century. It is the subject of the 'law' of Delpech[2] and the related, almost forgotten, 'law' of Guerin.[3] Delpech states that (author's translations): '...the conservation of the mass and energy of muscles, depends partially on the right degree of tension that nature wanted to give them and that the deformity has changed'[2] while Guerin states: 'That the largest number of articular deformities of the osseous system in congenital malformations, the foetus and the infant are the direct product of the active retraction of muscles, caused by an lesion of the nervous system, either of the brain or the spinal cord or of the nerves'.[3] Both hypotheses are more aetiological than predictive laws, and each focuses on different sides of the same coin since in development and neuromuscular disorders neurons and

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muscle cells are interrelated. However, each law stresses a different factor as dominant in contracture formation: muscle mass and muscle energy (Delpech) or the primary nervous lesion (Guerin). Depending on the context, both could be true.

In children suffering from an obstetric brachial plexus lesion or Brachial Plexus Birth Injury (BPBI) contractures occur in 10% to 30% of the children[4] and reduced muscle fibre and muscle/tendon length have been found.[5,6] In the debate on the aetiology of these contractures, percolating through time, both hypotheses resurface. Both denervation and muscle function/imbalance have been tested in experimental studies on the pathophysiology of these contractures. Denervation leads in experimental studies to reduced muscle growth (hypotrophy) and contracture-formation.[7,8] The evidence for the role of muscle imbalance in contracture formation in experimental studies is conflicting.[7,9,10] The proposed mechanism is that if an agonist is weak, the antagonist is not stretched and normal growth is inhibited.[11] The weak external rotator is considered as a cause of the internal rotation contracture of the shoulder often present in a BPBI.[12] In longitudinal studies in children with a BPBI no relation between residual muscle function and elbow contractures has been found.[13,14] The aim of the present cross-sectional clinical study is, following the hypotheses of Guerin and Delpech, to test which factor is more related to flexion contracture formation of the elbow in children with a unilateral BPBI: the extent of denervation or residual muscle function/imbalance.

Patients and methods

Between 2008 and 2015 a total of 100 children (61 boys, 39 girls; mean age 10.4 years, 4 to 18) with a unilateral BPBI, visiting the multidisciplinary team for children with sequelae of BPBI, were included in the study. This study includes 16 patients from a previous longitudinal study on the relation between infant MRI findings and infant muscle function and childhood contractures and muscle force.[14] The right arm was affected in 60 children. In 58 children included in this study surgical plexus reconstruction in infancy had been performed according to standard criteria.[15] Excluded were children who could not cooperate with the muscle testing procedure and children with complete lesions (Narakas IV) because of extreme weakness of the upper arm muscles precluded force measurements.

Denervation and the extent of the neural lesion was classified according to Narakas[16] (class I: deltoid and biceps paresis, C5, C6 lesion; class II: deltoid and biceps paresis plus paresis of the extensors of elbow, hand and fingers, C5, C6, C7 lesion; class III: almost complete paresis, C5, C6, C7, C8 lesion. Children of class IV (total arm paresis, Horner syndrome, C5, C6, C7, C8, Th1 lesion) were excluded.

Upper arm muscle peak-force was measured with the Microfet 2 dynamometer (Biometrics, Almere, The Netherlands) on both the affected and normal side. Measurements were performed by the same orthopaedic surgeon for each child (JAS). During isometric measurement the children are standing with their arm along their body and the elbow at the waist. While the elbow is held at 90° flexion along the body (waist), hand pointing forward, the dynamometer is positioned at the wrist. The children are asked to exercise maximal pressure to the dynamometer for flexion and extension of the forearm. Each measurement is repeated three times and the median value is used and reported in Newtons (N). The flexion and extension force of the upper arm muscles were measured in Newtons at the wrist and are further referred to as flexion and extension force. These forces are delivered at the wrist by the upper arm muscle acting through the lower arm which acts as a lever arm. Since the aim was to study the effect of muscle balance on contractures and since measurement errors of the elbow-wrist distance would add further 'noise' to the measurement's 'signal', no attempt was made to measure joint torque or to correct for the effect of wrist deviators on flexion force.

The maximum degree of active extension or minimum degree of active flexion of the elbow, when a flexion contracture was present, was measured with a goniometer after active, gravity-assisted positioning of the affected arm in maximum extension.

Statistical analysis

All data were analyzed using SPSS (version 15.0; SPSS Inc., Chicago, Illinois). Results are presented as means with SD. To correct for individual differences (like size and age), upper-arm force of the affected side is also expressed as paresis, that is a percentage of the values of the unaffected side.

The ratio of force of flexors and extensors is presented as median because some near zero values for extensors result in extreme values in ratio. Differences were tested, using paired *t*-test for asymptotic and distribution-free tests for data not having a Gaussian distribution: the Wilcoxon Rank sum test for paired data between the affected and unaffected arm and the Mann-Whitney U test for comparing measurement in subgroups. Correlations were tested with Spearman's Rho correlation coefficient. All tests were two-tailed and considered significant if $p < 0.05$. Normality was tested using the Kolmogorov test, showing that many parameters were not normally distributed. Age, paresis of flexion (percentage of unaffected side) and paresis of extension force were normally distributed.

To assess the role of a combination of parameters on contracture formation, multivariate analysis was performed with these normally distributed parameters, prior surgery (yes/no) and Narakas class (Narakas I *versus* II and III) which were used as binary parameters. The rational for comparing Narakas I *versus* Narakas II and III was that in Narakas I the triceps is more or less intact whereas in Narakas II and III the triceps is affected. This was used as a proxy for the extent of denervation of the muscles.

A *post hoc* power analysis showed that sufficient power was achieved for the correlation analysis of the flexion contracture with a power of > 80% (alpha = 0.05). The sample size has a power that allows detection of correlations R = > 0.28. For finding differences in means between flexion contracture in children with/without prior neurosurgery/ with Narakas I *versus* Narakas II and III, the sample size has 80 % power of detection of differences of > 10°.The study was approved by the Medical Ethical Examination Committee of our institution (number 2013/274) and informed consent was obtained from the infants' parents.

Results

Children were divided over the Narakas classifications as follows: I = 57; II =13; III = 30. The mean flexion contracture was 25° (90° to -5°). An overview of the contractures and muscle function measurements is shown in Table 1. In the affected arm both extensors and flexors were weaker compared with the normal arm and flexors were more affected than extensors (Fig. 1).

Table 1 Overview of results of 100 Brachial Plexus Birth Injury children showing measurements of unaffected and affected upper arm, ratio affected/unaffected of force measurements and ratio flexor/extensor force at the wrist. Values given as mean (SD)

	Affected arm (n = 100)	Unaffected arm	Ratio affected/unaffected, median (range)	Mean difference (95% confidence interval)	p-value (Wilcoxon test)
Flexion	128° (13°)				
Extension	-25° (19°)				
Flexion force (N)	49 (32)	103 (48)	0.47 (0 to 1.4)	54 (47 to 61)	< 0.001
Extension force (N)	47 (27)	79 (36)	0.67 (0 to 1.1)	31 (25 to 38)	< 0.001
Ratio flexion/extension force, median (range)	1.03 (0 to 16)	1.3(0.9 to 2.2)			0.001

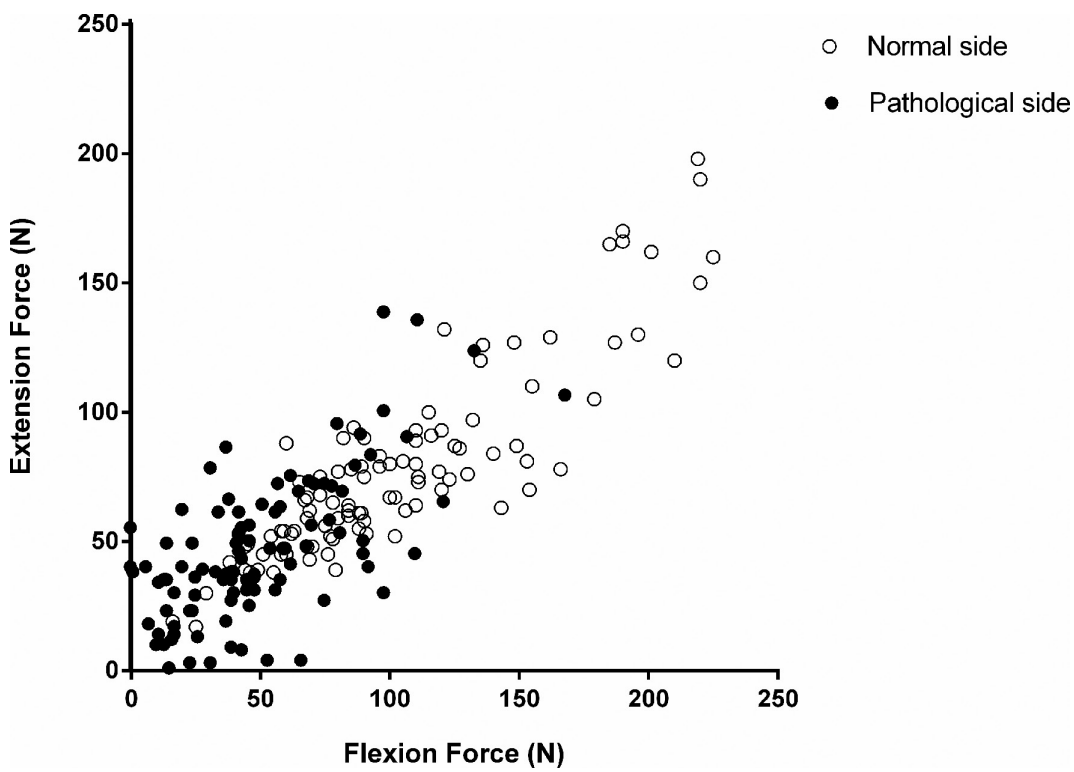

Fig. 1 The relation between flexion and extension force at the wrist (N) in affected (•) and unaffected (○) elbows (n = 100).

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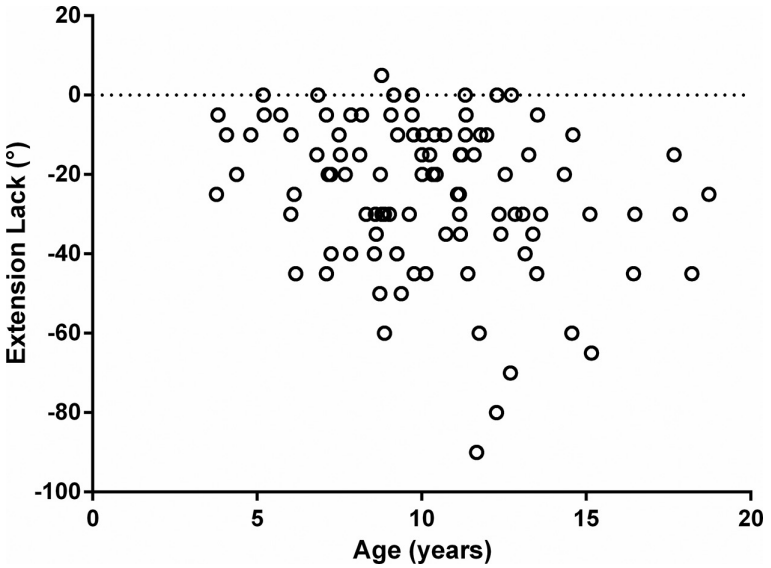

Fig. 2 Relation between age (years) and flexion contractures of the elbow in unilateral Brachial Plexus Birth Injury (Rho = -0.3, p = 0.008).

Table 2 Factors associated with elbow flexion contractures in Brachial Plexus Birth Injury (univariate analysis) values given as mean (95% confidence interval)

	Number of children	Elbow extension	p-value
Narakas I	57	-19° (-14 to -23)	I vs II: 0.001 (MWU test)
Narakas II	13	-37° (-26 to -48)	I vs III: 0.007
Narakas III	30	-30° (-22 to -37)	II vs III: 0.26 I vs II/III: p = 0.001
Neurosurgery			
Yes	58	-30° (-23 to -34)	0.009 (MWU test)
No	42	-19° (-14 to -23)	
Age		Rho = -0.3	p = 0.008
Paresis flexor		Rho = 0.06	p = 0.6
Paresis extensors		Rho = 0.4	p = 0.000 (Spearman correlation test)

MWU, Mann-Whitney U test

Contractures versus neurology

There were more severe contractures in Narakas classes II and III when compared with class I. Flexion contractures were more severe in children who had been operated on (who had a higher Narakas class) than non-operated children (mostly Narakas I) (Table 2). Flexion contractures were related to age (Rho = -0.3, p = 0.008) meaning contractures were more severe in older children (Fig. 2).

Contractures and residual muscle function/imbalance

Flexion contractures were related to the severity of the extensor paresis expressed as percentage of the unaffected side but not to the severity of flexor paresis as percentage of unaffected side (Table 2).

On the affected arm, flexion contractures were related to a relative dominance of the flexors (Rho = -0.4, p < 0.001) but subgroup analysis showed that this relation was only present in the operated children (Rho =-0.59, p< 0.001) and was absent in the non-operated children (Rho = -0.1, p = 0.4).

Contractures and both neurology and residual muscle function

The influence of the combined effect of various parameters on contractures was assessed in a multivariate model with flexion contracture as a dependent parameter and as independent parameters: prior neurosurgery (yes/no), extent of neurology (Narakas class I *versus* II and III), age, paresis of flexors (percentage of the force of the unaffected side), paresis of extensors (percentage of the force of the unaffected side) and ratio between flexor/extensor force on the affected side (measure of muscle imbalance) as independent parameters. This showed that age, prior neurosurgery and paresis of extensors (percentage of force of the unaffected side) were all independent parameters influencing the contracture (p = 0.004) (model summary R = 0.56, p = 0.000).

The extent of the lesions (Narakas classification) and neurosurgery are interrelated since Narakas class II and III predominantly occur in operated children. In the multivariate model, neurosurgery had more influence and adding the Narakas classification would not improve the model. Thus in the multivariate model, Narakas class, significant in the univariate analysis, lost its contribution/significance.

As in the univariate analysis, paresis of the flexors and ratio of flexor/extensor force were not significant in this multivariate model.

Discussion

This study shows that elbow flexion contractures in BPBI are related denervation aspects of BPBI (prior neurosurgery, Narakas class) and are related to the severity of the extensor paresis and age. Disturbed muscle balance is not a factor: it is only significant for the operated children and it is negative in the multivariate model.

In the literature two theories are presented for the aetiology of contractures in BPBI. Echoing Guerin, the first is denervation. As stated above, denervation itself leads in experimental studies on growing animals to reduced muscle growth (hypotrophy) and contracture formation. It has been shown to cause contractures after experimental surgical denervation in shoulder and upper arm muscles.[7,8] Reversible botulinum induced experimental denervation also caused contractures.[17] The current study also found more contractures in children with more severe BPBI (higher Narakas class, children with neurosurgical reconstruction) which is related to the extent of denervation. That growth impairment is a factor is supported by the finding of the current study that contractures were related to age.

Following Delpech, the second factor implicated in contracture formation is the muscle imbalance theory:[1,2] in case of a pathologically weak agonist, the antagonist is not stretched enough and without this adequate stretching normal growth is inhibited. This theory is used to explain that in BPBI with weak external rotators, internal rotator contractures of the shoulder will develop.[12] In experimental studies on brachial plexus lesions it was found that internal rotator contractures develop if the external rotator was weakened by selective neurectomy. However, if the external rotator was weakened by resection no contractures developed.[10] If muscle imbalance is a relevant factor we would expect in the current study that extensors would be more affected than flexors, but in actual fact the reversal is found. Alternatively, we would expect the ratio of flexor force/extensor force to be related to the severity of the contracture, but this was only found in operated children and was absent in non-operated children. In addition, the multivariate analysis to correct for confounding found that ratio flexor/extensor force was not a factor influencing contracture formation.

Thus, the current study lends more support to the denervation theory than to the muscle imbalance theory. Our study confirms longitudinal and cross-sectional studies in BPBI which found no effect of imbalance in infancy on later contracture formation.[13,14]

Based on our findings and supported by the multivariate model we suggest the following scenario: the extent of denervation causes lack of growth. This is supported by the fact that contractures are more severe in the group indicated for neurosurgery and in the univariate analysis in the higher Narakas classes. This lack of muscle growth becomes more visible as the humerus grows. This is supported by the finding that contracture severity increases with age, since the impaired growth of the muscles likely becomes more apparent when children get older. With age the contractures are followed by capsular changes. It is possible that extensor weakness resulting in limited physiological stretching of the denervated flexors may play a secondary role in the causation of these contractures. Lack of stretching as a cause of reduced length growth of muscle has been described.[11]

Contrasting the shortening of the flexors, the lack of contracture formation in the extensors is intriguing: the triceps shows very little shortening. A speculative explanation could be the difference in pennation angle between triceps *versus* biceps and brachialis fibres (17° *versus* 0°).[18] The pennation angle would then modulate the effect of growth retardation.

This study has several limitations. We do not have a good parameter for denervation: Narakas class and neurosurgery are imprecise measures for denervation. We are unable to identify the role neurosurgery plays in the outcome of both the elbow contracture as the muscle function. In this series almost all non-operated children were Narakas I. This confounder is difficult to neutralize from Narakas class since Narakas class and neurosurgery are interrelated: higher Narakas classes occur predominantly in operated children. Both are a proxy for the 'severity' of the denervation. Thus while both are related to contractures in the univariate analysis, in the multivariate analysis only the influence of neurosurgery yes/no becomes apparent and Narakas class has no extra influence.

Added to this, the contractures are caused by the combined defect of muscle shortening and, at this age, capsular issues, and we are not able to separate their influence on the contracture. However, the premise is that contractures are first caused by muscular changes and later followed by capsular changes, meaning that the effect of capsular changes on the *severity* of contractures can be neglected.

Another limitation concerns the force measurement. With elbow contracture of 90°, measured elbow flexion is influenced by the mobilization of shoulder muscles. This was relevant for the two children in our study: one child had 90° contracture and another 80°. Apart from that, the chosen force measurement method results in a systematic error. The forearm is about 2.5% of one's body weight: assuming a standard child of ten years with a weight of 30 kg this yields a 0.7 kg forearm/hand, equivalent to about 7 N. These 7 N influence the measured muscle force. Flexion force would be increased, extension force decreased. Calculations show that correcting for this would influence the force measurement by about 10%. The paresis (affected side/unaffected side) would change by 5%: flexion paresis would be about 5% larger and the extension paresis about 5% less than measured.

The muscle balance, the ratio flexion/extension force, is more affected since the numerator (flexion) is increased and the denominator (extension) is decreased. Calculation shows that this will increase the muscle balance values on both the affected and unaffected side by about 20%.

The confounding by this systematic error affects the force, paresis and balance values: all values are changed to different levels. But, given its systematic character, this does not influence the correlations, multivariate model and conclusions.

Another limitation is that this is a cross-sectional study: it is also possible that the measured muscle balance has changed since in infancy and the balance we measure now, is different from that in infancy. It might be that muscle balance in infancy is more important for contracture formation. Given the multiple experimental studies showing a relation between muscle balance and growth retardation we think the current study does not mean that muscle balance is irrelevant for contracture formation but warrants more studies in infancy on the aetiology of contractures, studies which are at present scarce.

In conclusion, this study suggests that in BPBI contracture formation is predominantly related to denervation and secondary to age, and that muscle function/imbalance is not a dominant factor in its aetiology.

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COMPLIANCE WITH ETHICAL STANDARDS

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No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

ETHICAL STATEMENT

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Medical Ethical Examination Committee of our institution (nr 2013/274).

Informed consent: Informed consent was obtained from the infants' parents and from all individual participants included in the study.

ICMJE CONFLICT OF INTEREST STATEMENT

All authors declare that they have no conflict of interest.

REFERENCES

1. **Farmer SE, James M.** Contractures in orthopaedic and neurological conditions: a review of causes and treatment. *Disabil Rehabil* 2001;23:549-558.

2. **Delpech J.** *Chirurgie clinique de montpellier ou observations et reflexions tirees des travaux de chirurgie clinique*. Paris et Montpellier: Gabon et compagnie, libraires, 1823: 202.

3. **Guerin J.** Essai d'une theorie generale des difformites articulaires du systeme osseux, chez les monstres, le foetus en l'enfant. *Gazette medicale de Paris* 1842;10:737-743.

4. **Pondaag W, Malessy MJ, van Dijk JG, Thomeer RT.** Natural history of obstetric brachial plexus palsy: a systematic review. *Dev Med Child Neurol* 2004;46:138-144.

5. **Pontén E, Gantelius S, Lieber RL.** Intraoperative muscle measurements reveal a relationship between contracture formation and muscle remodeling. *Muscle Nerve* 2007;36:47-54.

6. **Hultgren T, Einarsson F, Runesson E, et al.** Structural characteristics of the subscapularis muscle in children with medial rotation contracture of the shoulder after obstetric brachial plexus injury. *J Hand Surg Eur Vol* 2010;35:23-28.

7. **Weekley H, Nikolaou S, Hu L, et al.** The effects of denervation, reinnervation, and muscle imbalance on functional muscle length and elbow flexion contracture following neonatal brachial plexus injury. *J Orthop Res* 2012;30: 1335-1342.

8. **Nikolaou S, Liangjun H, Tuttle LJ, et al.** Contribution of denervated muscle to contractures after neonatal brachial plexus injury: not just muscle fibrosis. *Muscle Nerve* 2014;49:398-404.

9. **Soldado F, Fontecha CG, Marotta M, et al.** The role of muscle imbalance in the pathogenesis of shoulder contracture after neonatal brachial plexus palsy: a study in a rat model. *J Shoulder Elbow Surg* 2014;23:1003-1009.

10. **Nikolaou S, Peterson E, Kim A, Wylie C, Cornwall R.** Impaired growth of denervated muscle contributes to contracture formation following neonatal brachial plexus injury. *J Bone Joint Surg [Am]* 2011;93-A:461-470.

11. **Goldspink G.** Changes in muscle mass and phenotype and the expression of autocrine and systemic growth factors by muscle in response to stretch and overload. *J Anat* 1999;194:323-334.

12. **Hale HB, Bae DS, Waters PM.** Current concepts in the management of brachial plexus birth palsy. *J Hand Surg Am* 2010;35:322-331.

13. **Ballinger SG, Hoffer MM.** Elbow flexion contracture in Erb's palsy. *J Child Neurol* 1994;9:209-210.

14. **van der Sluijs MJ, van Ouwerkerk WR, van der Sluijs JA, van Royen BJ.** Elbow flexion contractures in childhood in obstetric brachial plexus lesions: a longitudinal study of 20 neurosurgically reconstructed infants with 8-year follow-up. *J Brachial Plex Peripher Nerve Inj* 2015;10:e15-e22.

15. **van Ouwerkerk WJ, van der Sluijs JA, Nollet F, Barkhof F, Slooff AC.** Management of obstetric brachial plexus lesions: state of the art and future developments. *Childs Nerv Syst* 2000;16:638-644.

16. **Narakas AO.** Obstetrical brachial plexus injuries. In: Lamb D, ed. *The Paralysed Hand.* Edinburgh: Churchill Livingstone, 1987:116-135.

17. **Kim HM, Galatz LM, Patel N, Das R, Thomopoulos S.** Recovery potential after postnatal shoulder paralysis. An animal model of neonatal brachial plexus palsy. *J Bone Joint Surg [Am]* 2009;91-A:879-891.

18. **Murray WM, Buchanan TS, Delp SL.** The isometric functional capacity of muscles that cross the elbow. *J Biomech* 2000;33:943-952.