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Management of Pediatric Patients with Spina Bifida

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Abstract

Spina bifida is a neurodevelopmental disorder and belong to most common congenital malformations. It is a neural tube defect that originates within first 28 days after conception. Although survival rate of these patients had changed rapidly within last decades, neural tube defects are still cause of substantial part of children morbidity. Occult type of spina bifida is a simple nonunion of vertebral arch without causing any symptoms. Open defects according to degree of involvement of neural tissue cause symptoms such as paralysis of lower extremities, bladder and bowel morbidity, delay in development of cognitive functions of various severity and other possible complications affecting morbidity of these patients. Early diagnosis and treatment of open spina bifida and accompanying complications is crucial and largely affects the outcome. Successful treatment requires lifelong cooperation of a whole range of specialists and guiding of treatment by primary care doctor. Survival and quality of life are associated with access to proper medical and surgical treatment as well as community support systems. This chapter offers overview of this topic with emphasis on general management of patients suffering from this congenital malformation.

Keywords: spina bifida, spinal dysraphism, management, spina bifida occulta, myelomeningocele, meningocele

1. Introduction

Developmental defects belong worldwide to leading causes of infant morbidity. Special interest deserve neural tube defects, that comprise anencephaly, spina bifida and encephalocele.

Spinal dysraphisms comprise a broad spectrum of congenital disorders resulting from impaired structural development of the craniospinal axis during brain and spinal cord growth and differentiation within 2nd and 6th week of gestation and proceed through a complex multistep process [1].

Spina bifida is a group of developmental disorders of neural tube. Neural tube in developing embryo forms future brain, spinal cord and their supporting structures. Under normal circumstances neural tube closes on 28th day after conception. In children with spina bifida neural tube does not develop or close properly causing dorsal defect of spine or spinal cord itself. Severity of symptoms and possible complications depends on location, size and type of defect.

Spina bifida is a complex disorder that requires multidisciplinary approach in diagnostics, treatment and complications solving.

2. Types of spina bifida

Spina bifida or spinal dysraphism is a wide spectrum of clinical and imaging findings concerning incomplete fusion of the midline neural and bony structures during early embryogenesis. Spina bifida can be devided into closed and open forms (Table 1).

Closed spinal dysraphism (spina bifida occulta or occult spinal dysraphism) is the most common type. This group of dysraphisms refers to broad spectrum of skin-covered congenital defects caused by non-union or failure to fuse of the neural tube. Clinical manifestation can range from asymptomatic simple non-union of vertebral arch taht is usually diagnosed as an incidental finding on imaging and causes no symptoms to more severe forms with progressive neurological deteriora-tion. Closed spinal dysraphism can bez present with or without subcutaneous mass.

To closed spina bifida without subcutaneous mass belong: tethered spinal cord, dermal sinus, diastematomyelia and spinal lipoma. Closed spinal dysraphism with subcutaneous mass are: lipomyelomeningocele, lipomyelocele, terminal myelocys-tocele, meningocele, non-terminal myelocystocele.

Tethered spinal cord characterized by abnormal attachment of spinal cord to surrounding structures causes traction of spinal cord during growth and its ischaemisation leading to progressive motor deficit, urological and ortopedical complications [2].

Dermal sinus is a median or paramedian epithelial duct causing persistent communication connecting spinal cord with skin. It is a consequence of incom-plete separation of the ectoderm from the neural crest. It is usually visible during aspection as a small pit in lumbosacral area often connected with hpertrichosis or hyperpigmentation. The duct can terminate in the soft tissue overlying spinal canal, in epidural space and, in most of the cases, directly on conus medullaris, cauda equina or fillum terminale. Newborn can display neurological deficit or can

Closed spinal dysraphism (CSD)
CSD with subcutaneous mass
Tethered cord syndrome
Dermal sinus
Diastematomyelia
Spinal lipoma
CSD without subcutaneous mass
Lipomyelomeningocele
Lipomyelocele
Terminal myelocystocele
Meningocele
Nonterminal myelocystocele
Open spinal dysraphism (OSD)
Myelomeningocele
Myelocele
Hemimyelomeningicele
Hemimyocele

Table 1.
Types of spinal dysraphisms [3].

develop neuroinfection. Because of direct communication between skin surface and spinal canal germ can easily spread and cause meningitis or intraspinal abscess. Ultrasonography is a useful accessible first-line imaging that can show the length of the sinus. Subsequently, MR imaging is necessary. In differential diagnosis is necessary to differentiate from sacro-coccygeal sinus that is located lower in sacral or coccygeal region and usually terminates in fascia and does not extend into sub-arachnoid space [3].

Diastematomyelia is also known as split cord malformation and it is a longitudinal split. It is mostly located between L1 and L3, less frequently between Th7 and Th12. This defect is divided according to a presence of dividing septum and single and double dural sac into two types:

Type I has common midline septum or spur, double dural sac and is symptomatic. Type II has both hemicords in a single dural sac [3].

Spinal lipoma is caused by premature separation of the ectoderm from the neural crest causing mesenchymal cells to get stuck within the spinal canal. Lipoma can be extradural or intradural or their combination. Lipoma is made of adipous tissue but also contain meningeal and neural cells [4]. These lesions can expand later during life because adipocytes can increase in size easily.

Spinal lipoma can be present in 3 forms:

Filum terminale fibrolipoma – filum terminale above 2 mm thick, hyperechoic on ultrasonography, often connected with tethered cord syndrome [3].

Intradural lipoma – usually lying along midline with completely formed and appropriately closed dural sac. In lumbosacral region causes often tethered cord syndrome and in cervical and thoracic regions lipoma usually causes compression of spinal cord with subsequent symptoms [5].

Lipomyelomeningocele and **lipomyelocele** belong to closed spinal dysraphisms that present as fat-containing subcutaneous mass beginning above gluteal cleft and extending caudally in asymmetrical position [3].

Myelocystocele is a closed spinal dysraphism with dilatation of central canal of spinal cord that protrudes dorsally into the subcutaneous tissue. Spinal cord terminates in a cyst [3].

Meningocele is protrusion of meninges through a defect in vertebral column. There is a visible sac filled with fluid on the back but without involvement of spinal cord. There is usually minimal or none neurological impairment.

Open spinal dysraphisms are developmental anomalies that are not covered by skin and are caused by unclosure of the neural tube during primary neurulation. They are mostly diagnosed during antenatal screening by ultrasonography and are also visible during newborn physical examination. To open spinal dysraphisms belong: myelocele, myelomeningocele, hemimyelomeningocele and hemimyelocele.

Myelomeningocele is the most common and most severe type of spina bifida occurring mostly in middle or lower back (but also more cranially) forming a sac on infant's back that contains open dural layer and improperly formed spinal cord or nerve radicles. Nerve structures are extruded into the fluid-filled sac – this is called spina bifida cystica. Vertebral arches are dorsally incomplete.

3. Epidemiology

Incidence of spina bifida varies worldwide between 1 to 10 per 1000 births [6] and between 0,17 to 6,4 per 1000 live births for myelomeningocele [7] but has differences in geographical regions with higher rates in less developed countries. In Europe it is around 4500 pregnancies a year that are affected by neural tube defect. Over 90% of more serious spina bifida cases is diagnosed before 22nd gestational

week [8]. Overall prevalence of spina bifida is lower in countries with mandatory folic acid fortification of grain products opposite to countries with voluntary or no fortification [9, 10]. More affected are females and whites and Hispanics.

4. Etiology and pathophysiology

Detailed etiology of spina bifida is not known but it is assumed to result from a combination of more factors - genetic, nutritional and environmental risk factors. Genetic risk factor is a family history of neural tube defect. Most important nutritional factor is folate deficiency. Even though exact mechanisms leading to spina bifida are not clearly known, there are some of researchers interest [11].

4.1 Folate deficiency

Folate is a natural form of vitamin B9. Its synthetic form is folic acid. Folate is important for proper intrauterine development of fetus. Its deficiency is connected not only with spina bifida, but also with occurrence of all neural tube defects. Spina bifida is significantly more common in countries without legislation regulating full-coverage folic acid fortification of the food supply and less common in world regions with mandatory folic acid fortification [9].

4.2 Positive family history of spina bifida

Genetic factors seem to play important role in etiology of spina bifida. Couples with child born with spina bifida are at higher risk of having another child born with this defect. At higher risk of having child affected by spina bifida are also women who were born with neural tube defect and also higher frequency is in twins than in singletons. All this indicates a genetic contribution to etiology. But low frequency of families with multiple neural tube defects makes research more difficult [11].

4.3 Medications

Some drugs are under suspicion in contributing to higher risk of developmental disorders of neural tube. Mostly anti-convulsants (anti-seizure medication), such as valproic acid, when taken during pregnancy. They probably interfere with metabolism and utilization of folate and folic acid.

4.4 Decompensated diabetes mellitus

Women with decompensated or inadequately compensated glucose levels during early stages of pregnancy are at higher risk of having child with spina bifida.

4.5 Obesity

Spina bifida and all neural tube defects are more common in women with obesity. It is important to have adequate body mass index also prior to pregnancy.

4.6 Hyperthermia

Increased body temperature in early stages of pregnancy due to infection or using of sauna is believed to be potentially risky for having a child with neural tube defect.

Women with present risk factors should be medicated with higher dose of folic acid preconceptionally and also during pregnancy. In women who use more risky medication (f.e. anti-seizure medication) should be pregnancy planed with switch of medication to more safe one.

5. Symptomatology

Severity of symptoms depends on type of spina bifida ranging from no symptoms in spina bifida occulta to most severe in myelomenigocele. There are also interindividual differences. Spina bifida occulta is neurologically asymptomatic because there is no involvement of neurologickal structures.

5.1 Skin lesions or visible sac

Cutaneous lesions mostly in lumbar region could be associated with spina bifida or tethered spinal cord. Visible change of skin above the defect is usually an abnormal tuft of hair, dimple, subcutaneous lipoma or a birthmark [12]. Such skin lesion could also be a symptom of spinal cord abnormality that is covered by skin.

Sacral dimple is a common skin lesion and is found in 1,8 to 7,2% of newborns [13]. However, in most of newborns it is only a simple skin lesion without any effect on neurological functions. Possitive ultrasonography findings are usually filar cyst (24,8%), echogenic filum terminale (13,5%) and low-lying spinal cord (11,7%). Some literary sources consider filar cyst as a normal finding [14].

Simple solitaire sacral dimple in asymptomatic newborn with diameter less than 5 mm located no more than 25 mm above anal opening have extremely low risk of having spinal abnormality [15]. Considering this very low risk (approx. 0,34%), more recent guidelines state that sipmple solitaire non risky sacral dimples do not require additional imaging – only in case they are atypical, associated with other skin lesions or multiple. On the other hand around 86% of spinal dysraphisms are associated with overlying cutaneous lesion [16].

Open defect is mostly situated in the lumbar region and is characterized by opened spinal canal along more vertebrae. At birth meninges, spinal nerves and spinal cord protrude above surrounding skin level forming a sac. This sac could be also covered by skin. These open defects are easily recognized whereas smaller or closed defects can present only by overlying cutaneous lesions [17].

5.2 Paraparesis

Degree of neurological impairment, walking disability and muscle weaknes depends on severity and extent of the defect, as well as on accuracy of prenatal or postnatal treatment. Neurological deficit varies from mild paraparesis to paraplegia. Myelomeningocele is the most common congenital anomaly causing physical disability [18].

According to level of defect there are various degrees of motor disability (**Table 2**). Patients with thoracic defect have flacid lower extremities, patients with high-lumbar defect usually can perform flexion in hip joint, in middle-lumbar defect also extension in knee, in low-lumbar defect is also foot dorsiflection present and sacral defect usually allows to perform also plantar flexion of foot [20].

Neurological deficit in patients with spina bifida is thought to be result of the primary insult - the congenital anomaly and the second - from direct exposure of spinal cord to amniotic fluid and intrauterine trauma [21].

Level of lesion	Muscle function	Ambulation
Thoracic High Lumbar	Lack quadriceps function	Children – ambulation with hip spanning orthosis (hip-knee- ankle – foot orthosis or reciprocating gait orthosis) Adults – majority require wheelchair
Low lumbar	Lack function of gluteus maximus and medius Retain quadriceps and medial hamstring function	Require crutches for ambulation Most retain comunity ambulation as adults
Sacral	Retain quadriceps and gluteus medius function	
High sacral	Lack gastrocnemius function	Ambulate with ankle-foot orthosis and no support
Low sacral	Retain gastrocnemius function	Ambulate without braces or support

Table 2.
Functional outcome according to level of spinal dysraphism [19].

In a study with 50 years follow up of walking ability half of the patients with severe spina bifida was able to walk for 50 m butthis ability declined with age to 27% in the age of 50 years [22].

5.3 Urinary dysfunction

Nerve damage in neural tube defect leads to loss of sensation and bladder sphincter control. Very common is neurogenic bladder that leads to symptoms such as urinary retencion, overflow incontinence, urgency, frequency and nocturia. Possible complications are incontinence, repeated or chronic urinary infections, hydronephrosis and in later stages renal damage [23] that all leads to diminished quality of life [24].

5.4 Bowel dysfunction

Most of patients living with the diagnosis of spina bifida have some degree of bowel problems called neurogenic bowel dysfuntion. The lack of bowel movement results in obstipation and lack of anal sphincter control leads to intermittent or continual incontinence [23]. Bowel dysfunction leads to decreased life quality [19, 25].

6. Complications

Possible complication affect in some degree most of patients with open forms of spina bifida. The severity of complications depend on extent of defect and also on timing of treatment. Fetal surgery gives better prognosis.

6.1 Hydrocephalus

The majority of infants with open neural tube defects also has hydrocephalus [26]. Hydrocephalus is defined as an active distension of the ventricular system resulting

from inadequate passage of cerebrospinal fluid at some point from its production within ventricles to its absorption into the systemic circulation [27]. In infants it is a condition with ventricular enlargement that leads to rapid growth of head circumference and requires surgical intervention [28]. According to observations only 1 out of 6 infants with myelomenocele has symptoms of raised intracranial pressure at birth and 1 out of 8 has head circumference above 98th percentile at birth [29]. Many infants develop ventriculomegaly that leads to increase of head circumference after postnatal closure of open spina bifida. Slight ventricular enlargement with stable neurological status could be indication for conservative observation – radiological and clinical. Rapidly developed ventriculomegaly with worsening of neurological status and signs of intracranial hypertension requires quick neurosurgical intervention [26].

Surgical treatment possibilities are insertion of ventriculo-peritoneal shunt and endoscopic third ventriculostomy with cauterisation of choroid plexus. Minority of cases is indicated for conservative treatment – only those with relatively stable ventriculomegaly [26]. Infants who underwent fetal surgical repair of myelomenocele were less likely to require ventriculo-peritoneal shunting [30].

6.2 Complications of ventriculo-peritoneal drainage

Presence of hydrocephalus in children with open spina bifida requires placement of ventriculo-peritoneal shunt in most of the cases. Proper function of shunt is inevitable. Unfortunately, shunt related complications are frequent – mainly shunt malfunction and infection. About 95% of patients who required shunt placement have to undergo at least one shunt revision [26]. Symptoms of shunt-related complications are: headache, irritability, confusion, somnolency, nausea, vomiting, feeding problems, fixed downward gaze, seizures. In case of shunt infections also symptoms like higher body temperature, redness along the shunt catheters, elevated blood parameters of infections.

6.3 Chiari malformation type II

Myelomenocele as the most severe open defect is almost invariably associated with this malformation. Chiari malformation type II is a group of disorders that includes herniation of fetal developing cerebellum upwards into the middle cranial fossa or downwards into cervical spinal canal. This malformation is often associated with other abnormalities such as: brainstem kinking, abnormal fourth ventricle location and syringomyelia [30]. The research on animal models shows that chronic intrauterine leakage of cerebrospinal fluid can lead to Chiari II malformation [31]. It is common brain malformation in children with myelomenocele. This malformation worsens the cerebrospinal fluid circulation leading to progression of hydrocephalus. Chiari malformation type II can present with rapidly present symptoms such as: breathing problems or apnoea, bradycardia, swallowing problems and other cranial nerves dysfunction when descending cerebellum presses on brainstem [26]. Under rare circumstances can lead to indication of decompression of craniocervical junction. Chiari malformation type II, its presence and severity can in huge extent determine the outcome of patients [26]. Chiari II malformation is significantly less severe in infants who underwent fetal surgery for myelomenocele [30]. Improvement of this malformation and subsequent decrease in hydrocephalus in children with prenatal repair of myelomenocele support the theory of relationship between continual intrauterine abnormal leakage of cerebrospinal fluid and subsequent development of Chiari II malformation and hydrocephalus and underline the importance of fetal surgery [26, 30].

6.4 Tethered spinal cord

Tethered spinal cord is a neurological disorder that is caused by abnormal attachment of the spinal cord to surrounding structures. In case of patients with myelomeningocele spinal cord is mostly attached to scar from previous operation [32]. Symptoms are caused by increased tension and stretch-induces dysfunction of the caudal spinal cord and conus and include motor and sensitive dysfunction, gait abnormalities, symptoms of cauda equina syndrome and urological symptoms [12, 32].

Filum terminale lipoma can cause cord tethering, lipoma is the most common cause of thick filum terminale. That is why detection of abnormal thickening of filum terminale is important. Initial detection is usually performed by ultrasonography [2] followed by MR imaging [12]. Tethered cord syndrome must be suspected when conus medullaris is placed dorsally in the spinal canal and terminates below the superior aspect of L3 vertebral body. Also thickened filum terminale can be present. MR imaging is indicated in ultrasonography evidence of tethered cord or in case of doubts [3].

Although some patients with anatomic cord tethering do not develop symptoms, most of the patients are symptomatic and do not naturally improve without surgical untethering. Neurosurgical intervention is the treatment of choice, though with varying results [33]. Timing of the surgery is also important – early intervention after symptom development is necessary for recovery or at least improvement of neurological functions. Early surgical intervention as a prevention of further neurological damage requires early diagnostics [12].

6.5 Meningitis

Infants with open neural tube defects can experience meningitis – inflammation of brain and spinal cord surrounding meninges. Meningitis could develop as a consequence of open defect, as a complication of surgical procedures as well as a complication of shunting procedures. In case of bacterial meningitis there is a need for massive antibiotic therapy.

6.6 Urological complications

Most of the patients with severe spinal dysraphism suffer from neuropathic bladder impairment [24]. As the nerve damage causes urological complication by means of neurogenic bladder, this situation also brings specific possible complications. Usual problem is urinary retention that could lead to overflow incontinence, renal damage and urinary tract infections, that could be repeated or chronic and often requires antibiotic treatment.

It is necessary to maintain proper urine derivation with no residual urine left. These patients require long time follow up by urologist. Urological complications and renal disease as a consequence is very common cause of higher morbidity mainly in older children and adults with open spinal defect. Severe bladder mortality is most frequently present in patients with huge spinal defects without covering membrane. This verifies the theory of increased damage of nerve roots from direct exposure to amniotic fluid [34].

6.7 Gastrointestinal complications

One of the most common problems of patient with spina bifida in adulthood is neuropathic bowel dysfunction with constipation and incontinence, but these patients also often suffer from dysphagia – mainly patients with brain stem compression.

Brain and spinal cord nerves modulate activity of enteric nervous system. Patients with severe and highly located forms of open spina bifida and resulting Chiari II malformation have impaired function of nerves leading to dysfunction of gastrointestinal tract mobility. Gastrointestinal problem that these patients suffer from is diminished bowel movements causing obstipation or opposite also diarrhea. Patients often suffer from anal incontinence from mild to severe degree [19].

Patients with large and high located myelomeningocele often suffer from dysphagia. Development of dysphagia in children with myelomeningocele is caused by cervicomedullary kinking and brainstem compression due to crowding in the posterior fossa in Chiari II malformation. Dysphagia leads to swallowing difficulties, feeding difficulties, failure to thrive, bronchopulmonary complications and later to peptic ulcer disease [34, 35].

6.8 Bronchopulmonal complications

Children with large and high located myelomeningocele display also other complications such as Chiari II malformation that often leads to dysphagia. Severe dysphagia causes swallowing and feeding problems that might cause complications as aspiration pneumonia, pulmonary disease, reactive airway disease, bronchiectasis, stridor or apnoea [35]. Although almost all children with open spina bifida live into adulthood, patient suffering with brainstem dysfunction leading to such bronchopulmonary complications are at higher risk of fatal complications [34].

Children with thoracic and thoracolumbar levels of defect might in some cases also have impaired function of the accessory respiratory muscles. They also often have scoliosis that could lead to reduced forced vital capacity of the lungs [36].

6.9 Orthopedic complications

Orthopedics deal in patients with spina bifida with congenital and acquired deformities. Because of weak muscles of spine and lower extremities, these patients with open spinal defects can present with variety of orthopedic problems. Most frequently occurring problems are: scoliosis, kyphosis, muscle contractions, bone and joints deformities, hip dislocation, abnormal growth and talipes (club foot) [37].

Scoliosis is present in almost all children with severe and highly located myelomeningocele. Children born without covering membrane of the defect tend to have neuromuscular imbalance and spinal cord tethering which are conditions leading to scoliosis. Severe paraparesis leading to full-time use of wheelchair also enables occurrence of scoliosis [34]. Scoliosis also leads to pelvic obliquity with subsequent changes in sitting balance and contributes to unequal pressure during sitting. This factor together with lack of sensitivity leads to skin breakdowns [36]. One of the most important factors for maintaining ambulation in adulthood is strength of quadriceps and hamstring muscles [11].

6.10 Latex allergy

Many patients with open spinal defects are at higher risk of latex allergy. This means allergic reaction to natural rubber and latex products. Symptoms could be mild – such as rash, sneezing, itching, conjunctivitis and rhinitis, as well as very severe condition – anaphylaxis, that is potentially life threatening situation. This is a potential reason for using latex-free gloves at labor and also at giving care to these patients. Latex allergy could also lead to perioperative complications [11].

6.11 Sleep disorders

Children and adults with open neural tube defects often suffer from sleep disorders, from which sleep apnoea is the most severe one potentially affecting life quality. These patients should undergo evaluation of sleep disorders.

6.12 Wound healing

Because of lack of skin sensitivity below the level of open spinal defect, patients do not properly feel small wounds or sores on their lower extremities, buttocks and back region. That is reason that these small wounds may develop into more severe wounds that are more difficult to heal and may sometimes cause generalized infection. Skin breakdowns are also consequence of friction and pressure related to the use of orthotic aids that assist in positioning and ambulation as well as constant pressure on insensitive skin due to immobility, especially with increasing body size and weight [38].

Many patients with open spinal defect have altered sitting balance due to paralysis of abdominal, thoracic and lumbar extensor musculature. Due to this imbalance together with insensate skin leads to frequent skin breakdowns [36].

6.13 Neurocognitive disorders and educational status

Many children with severe forms of spina bifida suffer from specific learning disabilities, such as dyslexia, dyscalculia, problems with paying attention. Patients with less severe forms of spinal dysraphism and with lower levels of defect have higher chance to obtain higher education and better employment and insurance status [19].

6.14 Psychological problems

Patients with open spinal defect prone more to develop depression or suffer from anxiety. Attaining early ambulation provides psychological benefits even if the child later becomes sitter [11].

7. Diagnostics

Early diagnosis of spina bifida is crucial. This applies to open forms. It is known that closed spinal defect that affects only vertebral arch is often just incidental finding without clinical correlate. Early diagnose of open spinal defect gives better chances for better prognosis and for fetal surgery. In some sever cases it could lead to decision of termination of pregnancy.

7.1 Prenatal diagnostics

Screening of neural tube defect is part of routine prenatal screening. Each pregnant women is offered to undergo screening tests. Widely used screening tests during pregnancy are blood tests fetal ultrasonography. In special cases can also amniocentesis be indicated. Fetal MR imaging is used to verified neural tube defect in cases when fetal surgery is planned.

7.1.1 Blood tests

Initial wide screening for neural tube defects is made by blood tests. It is important to know that this test can have false positive as well as false negative results.

7.1.2 Maternal serum alpha-fetoprotein (MSAFP) test

A sample of maternal blood is taken for this test. Test determines the level of alpha-fetoprotein (AFP) in maternal serum. This protein is produced by fetal tissues and in normal production only small levels of this protein reaches mother's bloodstream. In abnormally high production of AFP, higher level of MSAFP can be detected.

Normal MSAFP level does not absolutely exclude diagnosis of spina bifida. On the other hand high MSAFP levels could be caused by miscalculation of fetal age or multifetus gravidity. In case of positive MSAFP test it is usually repeated. If the level remains high there is an indication for further evaluation, usually by ultrasonography. AFP test can be a part of triple screen test that is used for screening of neural tube defects but also other organs abnormalities.

7.1.3 Fetal ultrasonography

This diagnostic tool is widely and successfully used screening imaging tool. It is also accurate tool for early diagnostics of open spina bifida. Morphological ultrasound is made three time during pregnancy in each trimester. The first two ultrasounds are most important for early diagnostics. First examination by ultrasonography is performed usually between 11th to 14th gestational week. Second trimester examination is usual between 18th to 22nd week and this imaging is most important for assessment of correct fetal morphology and evaluation of signs of present spina bifida or hydrocephalus [2]. More advanced ultrasonograph could detect also milder forms of spina bifida and in experienced hands could be also useful in evaluation of severity of defect. Children with higher spinal lesions on prenatal ultrasound have more serious motor impairment [20].

7.1.4 Amniocentesis

Amniocentesis could be indicated after positive ultrasonography. This test is performed by needle inserted transabdominally under ultrasound control to amniotic cavity to take a sample from amniotic fluid. Amniotic fluid can be tested for AFP levels. Cells from amniotic fluid are used for genetic examination to rule out genetic abnormalities causing spina bifida, although genetically associated spina bifida is rare. This needs to be taken into account in decision making as the procedure of amniocentesis carries also risks.

7.1.5 Fetal MRI

Fetal MR imaging is a powerful diagnostic tool for evaluation of neuroaxis. It plays an important role in prenatal diagnosis, treatment planning and follow up [39]. Fetal MRI is used for determining the level of spinal defect and for selection of candidates for fetal surgery [34]. Fetal MRI is used in cases where prenatal screening and ultrasonography is positive. Open spinal defect in higher levels of spine is more often connected with increased fetal ventricular size [40]. Morphological evaluation by fetal MR imaging provides valuable information for prognosis and possible complications. Higher defects are frequently associated with dysphagia and absence of membrane covering defect is commonly associated with scoliosis and high risk of severe bladder dysfunction. Location and size of defect correlates with severity of motor deficiency, patients with higher and larger defects are predicated for full-time wheelchair use. Length and width of defect of the body defect are measured as segment span and interpediculate distance [34].

7.2 Postnatal diagnostics

Ultrasonography is a safe and effective screening method that is commonly used in screening system of the newborns. It is noninvasive imaging method that does not require sedation of newborn without exposure to radiation [12]. Newborns with physiological finding on ultrasonography do not require any further imaging evaluation. On the other hand, positive finding on ultrasonography require more detailed imaging performed by MR imaging [41].

7.2.1 Ultrasonography

Ultrasonography is the first-line survey for the assessment of spinal cord abnormalities. During the first six months of life non-ossificated vertebral arches and cartilaginous posterior elements provide acoustic window for detained imaging of spinal canal with its content and surrounding soft tissues [17].

Ultrasonography of the spinal cord in infants is very effective tool for imaging of spine and spinal cord compared to postossification [3, 12]. Major indication of spinal ultrasonography in selected group of newborns is possible detection of tethered cord syndrome. Progress of ossification in time makes ultrasonography more difficult [12].

Indications for spinal ultrasonography in newborns are: cutaneous lesions on the back (such as hypertrichosis, subcutaneous lipoma, sacral sinus, sacral dimple), spinal deformity, neurological abnormality (paraparesis, neurogenic bladder or bowel dysfunction), spinal trauma during delivery and syndromes with associated compression of spinal cord [41].

Spinal ultrasonography is performed in infant in lying prone position with the upper body higher than lower and in flexed spine (curved over pillow). This position offers better acoustic window. Imaging is performed with linear transducer through longitudinal and axial plane scans from craniocervical junction to coccyx [3].

The main structures that must be identified are: conus medularis, filum terminale, cauda equina and spinal roots, central echo complex and subarachnoid spaces. Tip of conus medularis is in newborns usually located L1 and L2 interspace, occasionally on the level of superior end plate of L3. Filum terminale is a band of fibrous tissue that extends from the conus to the caudal end of spinal canal. At the level of L5 and S1 it should be less than 2 mm thick and should be predominantly hypoechoic with a bright hyperechoic periphery. Cauda equina and spinal roots must move according to the pulsatile production of cerebrospinal fluid, as the ultrasonography provides live image of the structures. Central echo-complex is train-line hyperechogenicity provided by the interface of the two margins of spinal canal. It needs to be detectable at all levels of spine and the space must be regular along entire extension. The subarachnoid space is anechoic and does not contain structures except spinal cord and nerve roots [3].

In order to avoid unnecessary further imagings it is important to know some anatomical variations that are considered physiological. Some of them are: mild thickening of the epidural fat, mild thickening of the filum terminale (between 1 and 2 mm), malformation of the coccyx with palpable prominence in the sacral region, transient dilatation of the central canal (usually disappears during the first weeks).

7.2.1.1 Persistence of *ventriculus terminalis*

Also known as fifth ventricle. It refers to mild cystic dilatation of the terminal part of spinal cord canal due to incomplete regression of embryonic ventriculus

terminalis in the conus medularis. This condition is usually asymptomatic, but in some patients could cause low back pain, sciatica or urinary bladder dysfunction [3].

7.2.2 Other imaging methods

As ultrasonography of the brain and spine is quick and good available it is the best diagnostic first-line tool. But for proper imaging of brain, spine and supporting structures for evaluation of extent of the defect, treatment planning and estimation of prognosis there is a need for use of other diagnostic methods. After detailed ultrasonography newborns with more severe spinal defects undergo MR imaging of spine. In open spinal defects with a risk of hydrocephalus newborns undergo CT or MR imaging of the brain according to clinical need with a detection of serious neuroimaging findings, such as ventriculomegaly, tonsillar descent, hind brain abnormalities, nodular heterotopia of gray matter and corpus callosum abnormalities – such as aplasia, hypoplasia/partial aplasia with or without dysplasia [23].

8. Termination of pregnancy

Termination of pregnancy with severe fetal anomalies is a controversial issue with many moral and ethical controversies. Indication for termination of such pregnancy is a medical decision but as well moral choice of mother or parents. This moral choice is affected by religion beliefs, legislation, cultural values and socio-economical status [42]. Around 40% of mothers decide to continue with pregnancy after diagnose of severe open spinal dysraphism [23].

9. Treatment

Treatment of spina bifida depends on severity of primary defect. Occult forms of spina bifida usually do not require any treatment. All other forms are indicated for surgical repair.

There has been a significant improvement of patient outcomes in the past 50 years because of multidisciplinary approach with an increased life quality of patients and prolonged life expectancy [43]. But though survival has changed significantly within past decades, there has not been significant improvement of neurological outcome [44]. In struggle to ameliorate the neurological outcome fetal surgery seems to be a promise. If fetal surgery is not indicated newborn needs to be operated soon after birth.

As the spina bifida is a complex problem, also treatment needs to be complex and include also treatment of complications.

9.1 Fetal surgery

Neurological deficit in patients with spina bifida is thought to be result of two circumstances – the primary insult is the congenital anomaly and the second is from direct exposure of spinal cord to amniotic fluid and intrauterine trauma. This hypothesis is the rationale for preventing secondary damage to spinal cord by fetal surgery [21].

Fetal surgery in fetus with open type of spina bifida, though risky, is a promising procedure in improvement of neurological outcome. This procedure has to take place before completed 26th week of gestation. Indication for fetal surgery is a result

of multidisciplinary decision. Fetal surgery should be performed only in centres experienced with fetal surgery equipped by neonatology intensive care unit. It requires cooperation of more specialists: pediatric neurosurgeon, gynecologist, fetal surgeon, fetal cardiologist and neonatologist. During this procedure uterus needs to be surgically exposed, opened and spinal cord and meninges of the fetus are closed and covered by skin. In some cases this procedure can be performed less invasively by means of fetoscope.

Prenatal surgery of fetuses with open spina bifida – myelomeningocele before 26th weeks of gestation leads to lower incidence of postnatal presence of Chiari II malformation or its lower severity and less amount of infants with myelomeningocele requiring ventriculo-peritoneal drainage for hydrocephalus. Other abnormalities accompanying Chiari II malformation – such as kinking of brainstem and dislocation of forth ventricle are less frequent in infants who underwent prenatal repair of myelomeningocele [30]. Children after fetal surgery are less likely to need mobility aids, such as crutches. But fetal surgery still remains a risky procedure with possible pregnancy complications such as preterm rupture of membranes and premature delivery before 34th week of gestation in almost half of the cases that underwent fetal surgery [30]. Persistence of Chiari II malformation with descendent herniation on MR imaging 6 weeks after prenatal repair is a predictor of need for postnatal surgical hydrocephalus treatment [45].

Since prenatal surgery might bring more favorable results but carries risk of premature birth, parents facing decision about prenatal versus postnatal repair, need to get reliable and up-to-date information to make this difficult and necessary choice [23].

9.2 Postnatal surgery

Myelomeningocele and meningocele if not treated prenatally, need to be surgically treated as soon as possible within the first days after delivery [46]. Early surgery gives better chances for good outcome. Another reason for early surgery is diminishing the risk of infection of exposed neural structures. During surgical procedure surgeon closes spinal cord and creates a meningeal layer around spinal cord and covers defect with muscular and skin layer. In case of newborn with symptoms of intracranial hypertension, ventriculoperitoneal shunt can be immediately implanted to treat hydrocephalus.

A meta-analysis of two prospective studies showed no significant difference in neurological outcome between prenatal and postnatal surgical repair, but suggested improved independent ambulation at 30 months of age in children following prenatal repair [47]. Surgical complications are cerebro-spinal fluid leakage, infection and wound healing complications [23].

9.3 Treatment of complications

As the irreparable nerve damage has already occurred during abnormal development all treatment modalities aim to minimize resulting neurological deficit and to treat complications and to exclude them from having impact on life quality and overall survival. Treatment of complications usually begins right after birth. Some patients require repeated surgeries.

Although advances in treatment of spinal defect, such as fetal surgery and active screening and early treatment of complications have rapidly changed survival of these patients, complications are main cause of mortality of myelomeningocele patients. Most severe complications with possible impact on survival are brain stem dysfunction, hydrocephalus, shunt related complications and ventriculitis in children and renal disease in later life.

9.4 Treatment of hydrocephalus

Hydrocephalus may be present at birth with symptoms of active hydrocephalus leading to raised intracranial pressure. In such conditions hydrocephalus needs to be treated immediately. In cases without acute symptomatic hydrocephalus could be initial decision of observation. In case of rising symptoms of hydrocephalus it needs to be treated. Typical procedure is insertion of ventriculoperitoneal shunt, in which cerebrospinal fluid is being drained to peritoneal cavity where it is resorbed. This shunt system consists of ventricular catheter, ventril with chamber and distal peritoneal catheter. This type of drainage is most common. If there is a contraindication for drainage of cerebrospinal fluid to peritoneal cavity, it can be rarely drained to pleural cavity, right atrium of heart through venous system and very occasionally to gall bladder. Newer method is endoscopic procedure – third ventriculostomy in cases with stenosis of Sylvian aqueduct with cauterisation of choroid plexus to minimize production of cerebrospinal fluid. Possible complications of shunt systems, such as malfunction or infection usually require shunt revision. During growth children usually require revision with prolongation at least once [23].

9.5 Bladder and bowel management

Patients with open spina bifida need to be regularly evaluated for bladder and bowel functions to minimize the risk of complications and organ damage. Regular blood tests, ultrasound, kidney function tests, urodynamic assessment and X-rays need to be performed.

Urinary and bowel complications are associated with diminished life quality of patients [25]. Degree of continence and management techniques differ by type of spina bifida and age of patient.

Urological management consists of medications, proper and sufficient urine derivation – using catheters to empty urinary bladder if necessary and some surgical procedures. Patients with overactive bladder may require anticholinergic medical therapy. Antibiotic medication for treatment of urinary infection and in indicated cases also as a prophylaxis [23, 24]. Some patient also require clean intermittent catheterisation – CIC [23]. Surgical procedures used in these patients are: bladder augmentation, continent cathetrizable urinary channel, cutaneous vesicostomy, bladder outlet operation for continence and urinary stone removal. Used bladder management techniques are: indwelling catheter, CIC, cutaneous vesicostomy, urostomy into external appliance, condom catheter and use of Credé maneuver. Some patients are left incontinent in diaper and some have spontaneous controlled voiding [24].

Urinary management also changes with age of these patients. Chance for spontaneous voiding decreases with age. Daily use of antibiotics as a prophylaxis is rare, but more common in adults. Almost half of patients uses antimuscarinic medication and this is more frequent in children and younger age groups. Alpha adrenergic receptor agonist and antagonist medication to improve continence and voiding is rare [24]. One fourth of adults have undergone bladder augmentation. Creation of continent cathetrizable channel (Mitrofanoff or Monti), cutaneous vesicostomy and bladder outlet operation are more common in adults compared to school children and adults. History of surgery for urinary stones is more prevalent in adult age group. Use of CIC is less frequent in school children than in older age groups and is more common in patients with severe open spinal dysraphism. Management by indwelling catheter, condom catheter, Credé maneuver or urostomy bag (incontinent diversion) is overall less frequent but from age groups is more common in adults. Patients with spina bifida are more likely to develop urinary stones and

this risk increases with age, so higher rate of urinary stone removal in adults is not unexpected [24].

Bladder continence is reported to increase by age. Around one third of patients is continent in school age but almost half of the patients in adult age [24]. Though urinary incontinence affects life quality, it has lower impact than bowel incontinence [48].

Bowel management consists of oral medications, antiemetics, suppositories and sometimes also manual derivation of stools by digital stimulation and disimpaction of stools. Other management possibilities are also use of standard rectal enema, cone enema and mini enema [19]. Though rarely, some cases are treated with anal plug [23].

Dramatic improvement of life quality of patients with severe anal incontinence, severe constipation and no anal control can experience with antegrade continence enema – ACE, that is minimally invasive surgical procedure [23].

Other surgical procedures for treatment of neurogenic bowel dysfunction are: cecostomy button or tube, cecostomy button closure, colostomy and ileostomy [19].

Type of used bowel management tool may also differ by age. Use of oral medication is low or insufficient in all age groups. Timed evacuation and suppositories are more used in small children and their use decreases with age. Standard rectal enemas are more used in school children and adults and less by adolescents. Cone and mini enemas are more used in school children and less by adolescents and adults. Antegrade enemas through a surgically created channel or a cecostomy button and tube are more used in adolescent age than in childhood and adulthood. Digital stimulation and disimpaction is used by small number of patients and mostly used in adults. Higher prevalence of colostomy is in adults. Ileostomy is less frequently performed [19]. Degree of continence and sufficiency of incontinence control has great impact on life quality of patients with spina bifida [19].

9.6 Treatment of orthopedic complications

The main goal of orthopedic treatment in patients with spina bifida is to correct deformities that may prevent the patient from using orthoses to ambulate during childhood [11]. Orthopedic complications are common in patients with spinal defects, mostly congenital and acquired deformities. Frequent congenital deformities are kyphosis, hemivertebra, teratologic hip dislocation, clubfoot and vertical talus. Acquired developmental deformities are related to the level of defect and are caused by muscle imbalance, paralysis and lack of sensitivity in lower extremities, such as contractures, calcaneus and cavovarus. Orthopedical complications may also be a consequence of surgical intervention – for example in postoperative tethered cord syndrome [11].

Orthopedical surgical interventions are most common within first 5 years of life, especially within the first year of life – mostly due to presence of congenital deformities that require surgical correction [38].

Deformities of **hip joint** are mostly contracture, subluxation and dislocation and also rotational deformity of the lower extremity, such as internal or external torsion. This deformity is a result of muscle imbalance and paralysis of the supporting muscles. Untreated deformity could lead to pelvic obliquity and compensatory spinal deformity.

Knee joint can be affected by flexion or extension contracture, valgus deformity or late knee instability and pain. Contractures are more common in patients with higher location of spinal defect. Flexion contracture is a result of gradual contracture of the hamstrings with contracture of the posterior knee capsule due to prolonged sitting and quadriceps weakness or spasticity of the hamstrings and

quadriceps weakness due to tethered spinal cord. Flexion deformity can be present in ambulatory and also non-ambulatory patients. Surgical release of the hamstrings, gastrocnemius and posterior capsule can decrease the angle of contracture and improve the ambulation.

Extension contractures are much less common and occurs secondary to unopposed quadriceps function in weak hamstrings, extensive bracing in extension or surgical treatment for flexion contracture, but most of the cases are congenital and often also with teratogenic hip dislocation or clubfoot. Initial treatment is usually serial casting attempting to achieve satisfactory knee flexion that is around 90 degree. If the contraction interferes with gait and is persistent, usually VY plasty of quadriceps is performed with good results. In non-ambulatory patients in whom the contraction causes difficulties with sitting, tenotomy of patellar tendon is an option.

Deformity of the knee joint is a result of static forces of positioning, fibrosis of the surrounding muscles, muscle imbalance around knee joint and fracture malunion. Valgus knee deformity is more common in patients with low-lumbar or sacral dysraphism and leads to instability, pain and acceleration of arthrosis in adulthood.

Torsional deformities of femur and tibia are frequent in patients with severe spinal dysraphisms and presents more severe problem for ambulatory patients. Femoral torsion is present normally in all newborns initially, but in children with severe spina bifida does not decrease with growth due to abnormal gait and activity. Tibial torsion is more common. Internal torsion is congenital and frequently associated with clubfoot and external torsion is acquired secondary to muscle imbalance. Initial treatment is usually ankle-foot orthosis with twister cables. If not successful, internal torsion of tibia can be treated by rotational osteotomy and severe cases of external torsion by internal rotational osteotomy of the tibia.

Foot and ankle deformities lead to problems with effective ambulation, cause difficulties with bracing and shoe wear, affect cosmetic appearance of foot and can cause skin irritation leading to pressure sores [49]. Surgical intervention is usually tendon excision or osteotomy for bony deformity followed by use of ankle-foot orthosis during day and splint during night. Arthrodesis in these deformities should be strictly avoided because stiffness resulting from fusion in combination with insensate foot can cause neuropathic skin changes [49].

Clubfoot is the most common foot deformity in spina bifida patients [50]. Factors that contributes to development of clubfoot are spasticity, intrauterine positioning, contractures and muscle imbalance. Treatment methods that could be used are: serial manipulations and long-leg casting to gradually correct deformity and tenotomy of the Achilles tendon followed by foot abduction bracing for several years. If this treatment is ineffective there is an indication for double osteotomy – closing wedge osteotomy of the cuboid with an opening wedge osteotomy of the medial cuneiform.

Equinus is also frequent deformity. Spasticity probably plays the most important role in its etiology. In prevention regular routine of passive stretching with a night-time ankle-foot orthosis is used. Surgical treatment is indicated in patients with unbraceable foot with skin breakdowns. Mild deformities respond to Achilles tendon excision, severe contractures require radical posterior release in the posterior tibiotalar and talocalcaneal joints.

Another contractures occurring in spina bifida patients are vertical talus, calcaneus or calcaneovalgus, ankle valgus, hindfoot valgus, cavus, varus and cavovarus [49].

More severe cases may require surgical repair – correction of ankle or foot deformity, correction of congenital foot deformity, correction of equinus contracture, tendon excisions, correction of scoliosis, osteotomy for correction of bony

deformity, osteotomy of femur, pelvic osteotomy, reduction of hip dislocation, release of contracture of hip or knee joint, spinal fusion and corrective osteotomies for scoliosis. Spina bifida patients are at higher risk of postoperative complications such as wound infection, delayed union or malunion, skin breakdowns and post-immobilization fractures. For post-surgical immobilisation custom-molded total body splint should be used and spica total body cast should be avoided [11].

Measures of muscle strength are key for surgical management of orthopedic patients [38]. Better functional effect in patients with spina bifida is a result of better understanding of impact of radiologically diagnosed deformities on functional effect within last decades and their earlier treatment as a prevention of deterioration [11].

9.7 Complications of mobility

Due to present paraparesis in almost all cases, patient usually need mobility aids, such as: crutches, braces, walkers or even wheelchair at least for some time during growth. These mobility aids together with regular physiotherapy can help the child to become more independent. For daily functioning some aids could be used such as walking frames, commode chairs and bath chairs.

According to functional mobility ambulatory outcome could be:

Community ambulator who walks indoors and outdoors for most activities and may need crutches or braces.

Household ambulator who walks only indoors with help of aids and may use a wheelchair for some activities.

Therapeutic ambulator who can walk only in therapy session, sometimes with help of apparatuses.

Nonambulator who exclusively uses a wheelchair for most of his activities [38].

Various factors affect ability to ambulate, most important of those are: level of neurological impairment, hip deformity, scoliosis, foot and ankle deformity, age and presence of obesity [11].

Almost all patients with severe forms of spinal dysraphism with exception of some patients with low sacral lesions will require use of orthoses in ambulation from indications, such as maintenance of alignment, prevention of deformity, correction of flexible deformity, facilitation of independent mobility and protection of insensitive limb.

In children with defect in thoracic and high-lumbar regions around age of 12 months if child controls head and neck position, usually standing frame is prescribed, later hip-knee-ankle-foot orthosis and reciprocating gait orthosis.

Patients with low-lumbar and sacral spinal dysraphism usually require solid ankle-foot orthosis as it substitutes for weak or absent ankle plantar flexors and dorsiflexors. Use of forearm crutches should be considered as well, as these patients often display weakness of hip extensors and abductors. Patients with internal or external rotational deformity can benefit from ankle-foot orthosis with twister cables. Also knee-ankle-foot orthosis can be used in patients with excessive valgus stress at the knee joint who are too young for correctional osteotomy.

9.8 Wound healing and prevention

Skin problems are very common in patients suffering from spina bifida [50]. As the skin sensitivity is affected in children and adults born with open spina bifida they are more likely to develop various skin problems. Blisters, soles, calluses and burns on lower extremities are frequent. When found late this skin problems can lead to serious problems of complicated healing.

The most common site of pressure sores are sacrum, ischial tuberosity, greater trochanter and feet. Severe complication of skin breakdown and pressure sores is osteomyelitis of the underlying bone. When wound does not heal with appropriate soft tissue care, underlying deep infection must be suspected and diagnosed by laboratory and radiograph findings. Antibiotic treatment is indicated, in more severe cases also surgical debridement. Last therapeutical opportunity in severe non-healing deep wounds causing sepsis is amputation with preservation as much length of the extremity as possible [49].

Parents and caregivers need to prevent bed sores – avoid lying on one side too long, prevent sun burns and regularly control skin of back and lower extremities at least once a day. In case of new orthosis even more often. In older children it is necessary to control if the shoes fit properly. Barefoot walking should be avoided, especially on rough and hot surfaces. Self-adhesive foam pads can be used over pressure points [49].

Interventions of plastic surgeon within first year of life are mostly skin flaps and skin grafts associated with spinal closure. Need for surgery due to complications of wound healing is increasing with age.

In case of more severe bad healing wounds there is sometimes necessary to perform surgical debridement of skin wound, incision and drainage of abscess, skin flap operations, flap grafts, skin grafting, reduction of callus and revisions of skin scars [38].

9.9 Sexual dysfunction

Because of nerve damage patients born with open spina bifida defect suffer from sexual dysfunction in adolescence and adulthood. This might affect their sexual life. But most of spina bifida patients are fertile and are able to have children. Women born with open spina bifida should plan their pregnancy and are recommended to take 4 mg of folic acid a day (normal dose is 400 mcg) a month prior to conception and during early stages of pregnancy.

9.10 Cardiometabolic dysfunction

Patients with spina bifida affecting mobility have higher risk of developing components of metabolic syndrome in younger age due to low physical activity. They often suffer from abdominal obesity, insulin resistance or dyslipidemia with its metabolic and vascular complications [51]. People with physical disabilities spend less time performing physical activities compared to their nondisabled peers [52]. Consequences of a sedentary lifestyle include physical deconditioning [53]. Physical exercise can improve metabolic dysfunction [51].

Overweight, obesity, high BMI, high waist circumference and percentage of body fat are more prevalent in patients with spina bifida and they also have reduced aerobic fitness and muscle strength [54]. Metabolic syndrome is more prevalent in spina bifida patients compared to nondisabled controls. They often display high levels of VLDL and overall cholesterol, triglycerides and low HDL, suffer from hypertension and insulin resistance [55].

Arterial diameters in these patients are reduced and sheer stress on the vascular wall is increased what predicts endothelial dysfunction [51].

9.11 Treatment of other complications

Patients with spina bifida often have post-operative complications, mainly infectious complications – wound and urinary infections, that require antibiotic therapy. According to frequent latex allergy in these patients, they should be operated and treated only in latex-free gloves in order to avoid severe anaphylactic reaction [11].

Special care must be taken to avoid pressure sores as due to lack of sensitivity and frequent hypomobility these patients are at higher risk of developing pressure sores and other wounds. All skin lesions in spina bifida have higher risk of getting infected.

Children with spina bifida often display precocious puberty and need to be examined by endocrinologist.

Due to frequent joint contractions, post-surgical immobilization and worse mobility these patients often suffer from osteoporosis and they are at higher risk of pathologic fractures. These fractures are more common in patients with higher level of neurological impairment due to more severe neurological deficit and this risk rises with age [11].

10. Prevention

As the effect of folic acid intake is known for its role in decreasing incidence of neural tube defects it has a great potential in prevention. Mandatory folic acid fortification has significantly higher effect on increasing serum folate levels than just recommendation [56]. Supplementation of folic acid starting at least one month prior to conception and continuing through the first trimester of pregnancy reduces the risk of neural tube defects. Because of the fact that many women discover their pregnancy within second months, what is late for prevention it is recommended for women in childbearing age to have long time daily supplement of 400 mcg of folic acid. Some foods such as: enriched bread, rice, cereals and pasta are fortified with 400 mcg of folic acid per serving. Except this also consumption of foods that are naturally rich in folate is recommended, such as: milk, egg yolks, avocado, citrus fruits and juices, beans and peas and dark green vegetables, as broccoli and spinach are.

Because of only available prevention of neural tube defects, that is also cheap and accessible, planned pregnancy is the best option. It is advised for women who plan pregnancy or are likely to get pregnant to have daily intake of 400 to 800 mcg of folic acid.

Fetal absorption of folic acid from mothers intake is better than absorption of folate from food. Combined with fact that most of the people do not have recommended intake of folate from diet rationale for intake of synthetic folic acid is high. There is an evidence, that proper intake of folic acid could lead to diminishing risk of also other developmental disorders – such as cleft lip, cleft palate and also congenital cardiac defects. Women who were born with neural tube defect themselves or have anamnesis of birth or pregnancy with fetus with neural tube defect should take higher doses of folic acid. The same applies for women with anti-seizure medication.

11. Initial management

Management of treatment of severe forms of spina bifida that require surgical intervention begins just after diagnosis. Prenatally diagnosed cases need to be referred to tertiary unit for further management. Usually first more detailed imaging is performed, genetic examination and screening for other congenital anomalies. Mothers with fetuses with spina bifida are referred to multidisciplinary team for pregnancy follow up, choosing the therapeutic strategy and timing of treatment in consensus with decision of instructed parents [23].

11.1 Delivery

All pregnancies with fetuses with more severe form of spina bifida are followed up in tertiary centres. Birth is usually scheduled from 38th week of gestation [23].

Babies with myelomeningocele tend to be in breech position. Breech position, cystic form of spinal defect or big sac are indications for cesarian section. This type of delivery is also performed for its timing during the day when all specialists are available and newborn can be immediately treated.

11.2 Postpartal management

Directly after the birth newborn with open spinal defect is admitted to newborn intensive care unit and strictly monitored and stabilized. Newborns need to be properly examined for presence of other congenital defects or birth trauma, as well as evaluation of severity of spina bifida symptoms.

Examination of the newborn should include identification of level of paralysis of each extremity, presence of visible signs of spinal defect (skin lesion, visible sac), deformities of extremities (such a clubfoot, hip or knee contraction or dislocation) [11].

If newborn with open spinal defect did not underwent fetal surgery, postnatal surgery is indicated as soon as possible – just after stabilization of vital functions within the first days after delivery [46, 57]. Usually closure of spinal defect is indicated first with subsequent monitoring of ventricle size and symptoms of intracranial hypertension or symptoms of decompensation of Chiari malformation. Newborns who present with severe symptoms of intracranial hypertension at birth require shunt placement immediately.

Infants with stable slight ventriculomegaly with normal neurological status who are indicated for observation for hydrocephalus need to be routinely controlled. Clinical examination consists of evaluation of neurological status as well as regular frequent measurements of head circumference, palpation of fontanelle and cranial sutures. Also radiological controls are necessary. Best accessible is routine imaging of brain ventricles via head ultrasound and in special circumstances also use of magnetic resonance imaging.

After stabile postsurgical course with stable slight ventriculomegaly and physiological neurological status with no symptoms of active hydrocephalus and decompensated Chiari II malformation, infant can be discharged to home with indication for frequent outpatient multidisciplinary evaluations. Weekly, later biweekly evaluations by neurosurgeon are necessary with active detection of symptoms of active hydrocephalus and decompensation of Chiari malformation. In some cases growth of head circumference will stabilize and follow normal growth curve and mild to moderate ventriculomegaly will be stable.

Criteria for later indication of ventriculo-peritoneal shunting are onset of symptoms of intracranial hypertension (irritability, headache, somnolency, troubles with feeding, vomiting, bulging fontanelle, fixed downward gaze, „sun-setting“ eye movements, bradycardia and sudden progress of head circumference), radiological finding of rapidly enlarged ventricles (via ultrasonography or MR imaging) and also worsening of Chiari II symptoms (abnormal eye movements, swallowing problems, apnoea or stridor). If these symptoms are present, infant should be immediately indicated for ventriculo-peritoneal drainage [58].

12. Follow up

Children with spina bifida, mostly open forms require very close follow up and observation for all possible problems. Most of the complications could be solved or at least properly managed to maintain adequate life quality. According to study with 50 years follow up 50% of patients born with myelomeningocele and surgically

treated after birth were able to walk 50 m at the age of 9 years and 27% at the age of 50 years. Mobility decreases in time partially due to obesity and deterioration of general health conditions [22].

12.1 General practitioner

The role of **general practitioner** – primary care doctor (pediatrician or family doctor) is very important. Doctor evaluates appropriate growth, indicates vaccination and general medical issues and coordinates medical care given by specialists. Patients and caregivers have to be properly instructed of the need of healthy life style, physical activity, precise monitoring of the skin status in order to prevent severe skin problems [59].

As most of patients with spina bifida thanks to advances in treatment reach adulthood there is a need for transition of health care to adult specialists [19]. Because the prevalence of obesity and metabolic syndrome is higher in these patients there is a need for careful monitoring of metabolic complications also in young patients [51].

Children and later also adult patients with diagnosis of open spina bifida after initial treatment need special treatment and follow up from various specialists:

12.2 Developmental pediatrician

This specialist should be part of the multidisciplinary team and survey the overall development of the child and indicate further examination of specialist when needed.

12.3 Neurosurgical controls

Child needs to be regularly controlled by neurosurgeon to evaluate proper function of ventriculoperitoneal drainage. Especially children with mild ventriculomegaly without symptoms of active hydrocephalus need regular controls so that in case symptoms develop could child immediately undergo surgery. Around half of the patients with open spinal defect undergoes other neurosurgical intervention in addition to initial spinal closure and half of these additional surgeries occur before 1 year of age – most common procedures are spinal closure, ventriculo-peritoneal shunt placement or shunt revision [38].

12.4 Neurology

All children after open neural tube defect with subsequent lasting neurological impairment need to be under supervision of experienced pediatric neurologist who controls motor functions, indexes progression of motor functions. In case of worsening of neurological functions there is a need for imaging – usually MR imaging for active screening of possible complications, such as tethered cord syndrome or decompensation of hydrocephalus, malfunction of drainage.

12.5 Urological controls

Each child after open spina bifida repair needs to be regularly evaluated by pediatric urologist. This evaluation consists of examination of kidney functions and urine derivation. Blood tests together with ultrasound and X-rays are often used, also other imaging techniques and urodynamic evaluation. Aim of this follow up is

active screening for urological complications to prevent further damage. Since the survival of spina bifida patients has changed during years and most of patients live into adulthood there is also a need for management and follow up subsequently by adult urologist [24].

- Sexual health and education
- Gastroenterologist controls

12.6 Orthopedics and orthotics

The role of orthopedics is to monitor and treat deformities, follow up after early treatment, also monitor spinal balance and deformity and help in evaluation of motor function. The follow-up periodic orthopedical examination should include assessment of motor functions, sensitivity, range of motion, spinal deformity and integrity of skin. Early treatment of deformity by casting, bracing and surgical treatment may prevent fixed bony deformity [49].

Orthotics should periodically control the motor and mobility aids to ensure that orthoses are appropriate, in good shape and do not cause any pressure points on the skin [11].

12.7 Rehabilitation medicine and physical therapy

Special rehabilitations are necessary for children with open neural tube defect to increase movement, flexibility and muscle strenght. Skilled physical therapist plays an important role in the early detection of subtle muscle imbalance which could lead to severe deformity if left untreated. Therapist should perform serial manual muscle testing as a part of the routine at least annual examination [49].

There is a need for close cooperation between physical therapist and parents and caregivers to teach them basics of rehabilitation to practice it at home. For older children summer camps and recreational facilities for disabled are possibility to improve their physical activity. Some patients are also able to participate successfully in sports and should do so [51]. Basic physical strategies focus on muscle strengthening exercises, orthopedic supports and assistive devices meant to aid ambulation and posture control. Lifting weights is recommended for adolescents and adults to maintain condition of muscles. As patients have limited use of lower extremities, exercise has to rely on upper extremities and trunk. There is a potential for physical therapist to cooperate with local sport clubs and fitness centres to develop activity programs and supervise them [51]. Physical activities offer possibility to prevent other problems, such as obesity, metabolic problems or depression [52].

12.8 Psychologist and occupational therapy

Spina bifida patients have to face a lot of barriers to lead conventional life. As a result of physical disability, life-style, their environment and combination of these factors these patients are at higher risk of depressive disorder [60]. Teenagers, adolescents and also adults might feel isolated from their peers and have low self-esteem. They might feel worried, stressed, anxious or sad. If the feelings last for long time they might lead to depression. Occupational therapy and psychotherapy might help, as well as physical exercise. Daily physical activity is positively correlated with quality of life [51]. In serious cases consultation of psychiatrist might be necessary.

12.9 Neurocognitive rehabilitation

Many of children affected by open spina bifida, mostly those with implanted shunts to treat hydrocephalus have problems with concentration, hyperactivity, work slowly.

12.10 Special education teachers

Many children born with open spina bifida do not have problems at school. Children that present with some neurocognitive problems and special educational problems such as dyslexia or dyscalculia might profit from special education. Cognitive problems are more common in children who have hydrocephalus. Children at school need individualized educational plan with assistance. This plan is a result of cooperation of parents, teachers, school psychologist, school nurse and physical education teacher.

Patients with less severe forms of spinal dysraphism and lower level of spinal defect tend to reach higher educational effect. This is partially due to better mobility of these patients but very important factor is also bowel continence degree. Patients with bowel continence or sufficient incontinence control usually reach higher educational degrees, have higher employment and insurance status and are more likely to be independent, as educational status and employment are major determinants of health insurance status in adults [19]. Urinary incontinence does not have that impact on educational status as bowel incontinence. Bladder incontinence (particularly low-volume) has usually lower impact on overall life quality, educational status and employment than bowel incontinence [24, 48].

12.11 Social workers and social contact

There is an urgent need for adequate social contact of these children. Participation in sports and physical activity with peers improves social contact and life quality. Families can also contact Intervention programs for patients with spina bifida that work in many countries. Children with spina bifida meet a lot of barriers in access to various activities and have to rely on adults to organize and supervise activities [51].

12.12 Dietitians

Proper diet is important to avoid complications mainly according to bowel function. With a help of dietitian can parents and caregivers find the best dietetic tools for each individual child. Addition of dietary fiber can help to maintain regular stool. Enough water intake is important in prevention of obstipation and urinary infection. Proper dietary intake together with physical exercise helps to prevent overweight and obesity that could lead to metabolic syndrome and cause later metabolic and cardiovascular complications [51].

13. Prognosis

In the 1950s the survival rate of patients with most severe form of spina bifida – myelomeningocele was about 10% [61]. In the last decades, the multidisciplinary approach to care of spina bifida patients, has significantly improved patients outcomes. Recently, thanks to advances in medical and supporting treatment almost all children born with spina bifida survive into adulthood. There has been increase in

life expectancy and gain in the quality of life of spina bifida patients but also of their caregiver's life [43]. But unfortunately, neurological outcomes of spina bifida patients did not change significantly over the years of medical progress [44]. That is mostly due to fact, that the neurological impairment is mostly caused by primary damage from congenital spinal abnormality and also secondary due to exposure of nervous tissue to amniotic fluid [21].

Important factor for prognosis is ability to attain early ambulation. It provides physiological and psychological benefits even if the child will later become a sitter. Also patients with high-level spina bifida who participated in walking program have lower risk of fractures, pressure sores are more independent than those who had been prescribed wheelchair early [11].

According to long term follow up study median survival of myelomeningocele patients was 50 years. 34% of patients had died before 5 years of age. Most common cause of death was cardiorespiratory, neurological and urological complications, then hydrocephalus and infections of central nervous system, other causes are significantly less frequent [22].

Most of the survivors had IQ over 80 points. Only one fifth was fully continent without need of incontinency aids. One third of patients recorded chronic back pain.

Percentage of patients living independently on their caregivers raises in time after age of 25. Independent living at the age of 50 years is more common in patients without anamnesis of intracranial hypertension and without cerebrospinal fluid shunt revisions [22]. Increase of independent living with age might be partially due to fact that longer survival is associated with less severe primary defect.

14. Conclusion

Spina bifida occulta is usually an incidental finding with no effect on life quality. On the other hand, the most severe form myelomeningocele is a complex problem. Due to many complications threatening patient with this complex health issue, there is an essential need for multidisciplinary approach to monitor, prevent and treat possible complications that have impact on functionality, life quality and survival. Parents and close caregivers have crucial role in whole multidisciplinary team. They need to know how to manage child's situation and give child social and emotional support. Raising the child in caring environment could help to develop into young adult who is able to fight basic life issues: to care about his own health issues, going to school, working, finding and using transportation, living in their own and having a healthy relationship and family.

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