



Richard M. Pauli, M.D., Ph.D.,
Midwest Regional Bone Dysplasia Clinics
revised 8/2009

MULTIPLE EXOSTOSES NATURAL HISTORY

INTRODUCTION:

The following summary of the medical expectations in Multiple Exostoses is neither exhaustive nor cited. It is based upon the available literature as well as personal experience in the Midwest Regional Bone Dysplasia Clinics (MRBDC). It is meant to provide a guideline for the kinds of problems that may arise in individuals with this disorder, and particularly to help clinicians caring for a recently diagnosed person. For specific questions or more detailed discussions, feel free to contact MRBDC at the University of Wisconsin – Madison [phone – 608 262 6228; fax – 608 263 3496; email – modaff@waisman.wisc.edu].

Multiple Exostoses, also called Hereditary Multiple Osteochondromata, is a relatively rare disorder, thought to arise in around 1 in 50,000 individuals. It results in the development of abnormal, benign, bony growths. These exostotic growths most often arise in the long bones and most often in the metaphyseal regions (near the ends of growing bones). Exostoses can involve virtually all bones, but invariably spare the skull and the face.

In those with a positive family history, radiologically demonstrable exostoses are virtually always present by 1 year of age. Therefore, in family members at risk we recommend that a complete skeletal survey be obtained at that age in order to determine if a new child is or is not affected. Even prior to this time many families will make a tentative diagnosis by palpating pea size exostoses in an affected child (most commonly along the medial or superior border of the scapulae, along the ribs, or along the tibiae).

Exostoses continue to grow during the period of the affected individual's growth. That is, exostoses may continue to appear and grow throughout childhood, tend to show a spurt of activity during adolescence and become dormant following completion of puberty. Indeed, any increase in size of an exostosis in adult life should precipitate additional evaluation regarding possible malignant transformation.

Multiple Exostoses does not just result in these benign tumors, but has a more generalized effect on bone development. Therefore, the complications that can be anticipated not only relate to the direct effects of the exostoses themselves but also because of effects on growth of bone. The number of exostoses present in an individual appears to be a good placeholder for the probability and frequency of serious sequelae in that individual.

MEDICAL ISSUES TO BE ANTICIPATED

PROBLEM: GROWTH

EXPECTATIONS: Initial growth is often normal. Slowing of growth may be seen in some in late childhood. Adults range from average statured to moderately short statured, with adult heights ranging from about 150 to 190 cm (4 feet 11 inches to 6 feet 2 inches) in males and about 130 cm to 175 cm (4 feet 3 inches to 5 feet 8 inches) in females. Most adults are within the normal range, while about 40% will be below the 5th percentile.

MONITORING: There are no growth charts available. Plotting linear growth on regular growth standards may provide some guide to whether growth velocity is being maintained.

INTERVENTION: There is no known treatment. Reassurance is usually appropriate.

PROBLEM: EFFECTS OF EXOSTOSES - COSMESIS

EXPECTATIONS: On average an individual with this disorder will develop around 20 exostoses. There is no justification for attempting to remove all of these. However, complications - either medical or cosmetic - may be sufficient that excision is needed. Affected individuals should be made aware that exostoses will never affect the face or the skull. The possibility of cosmetic removal should be explored anticipatorily.

MONITORING: -

INTERVENTION: Removal of exostoses only when clearly desired by the affected individual.

PROBLEM: EFFECTS OF EXOSTOSES - RECURRENT IRRITATION AND RECURRENT TRAUMA

EXPECTATIONS: Some sites may make for painful, recurrent irritation of exostoses – such as beneath a bra strap, beneath the waistband of underwear, along the medial edges of the proximal tibiae where rubbing occurs with walking. Some superficial exostoses may be subject to recurrent trauma that may result in pain, fracture and/or the development of a bursa and functional bursitis.

MONITORING: By history.

INTERVENTION: Excision is reasonable if recurrent irritation or trauma arises.

PROBLEM: EFFECTS OF EXOSTOSES - PRESSURE ON ADJACENT VESSELS

EXPECTATIONS: Vascular compromise to an extremity arises in perhaps 10% of affected individuals during their lifetimes. It is most common in the popliteal fossae.

MONITORING: By history. Various imaging methods sometimes are useful in assessing vascular compromise.

INTERVENTION: Excision is reasonable if vascular complications develop.

PROBLEM: EFFECTS OF EXOSTOSES - PRESSURE ON ADJACENT NERVES

EXPECTATIONS: Perhaps 15-20% of affected individuals will experience nerve compression during their lifetimes. Most commonly this results in sensory changes.

MONITORING: By history and neurologic clinical assessment if symptoms develop.

INTERVENTION: Excision is reasonable if symptoms are significant.

PROBLEM: EFFECTS OF EXOSTOSES - INTERFERENCE WITH JOINT FUNCTION

EXPECTATIONS: Frequency is unknown. Probably this most commonly arises with large, sessile exostoses of the pelvis and proximal femora causing limitation of hip movement.

MONITORING: By history and periodic clinical assessment. Radiologic evaluation should be undertaken if changes in gait, pain with hip movement etc. arise.

INTERVENTION: Excision.

PROBLEM: EFFECTS OF EXOSTOSES - PRESSURE ON SPINAL CORD

EXPECTATIONS: About 10% of affected individuals have vertebral exostoses, but often these are asymptomatic. Pressure on the spinal cord is a rare but potentially serious complication, reported in more than 50 instances thus far but probably affecting only around 1% of affected individuals. Usually it is within the cervical spine.

MONITORING: History of cervical myelopathic features or abnormalities of neurological clinical examination consistent with a cervical myelopathy should precipitate obtaining plain cervical spine radiographs and imaging of the region (with both computerized tomography and magnetic resonance imaging aiding considerably in defining if there is a compressive exostosis).

INTERVENTION: Surgical excision early in the course of this complication can result in reversal of the neurologic symptoms.

PROBLEM: EFFECTS OF EXOSTOSES - MALIGNANT TRANSFORMATION

EXPECTATIONS: Lifetime risk is probably only about 2%. Malignancy virtually never arises in childhood, usually is diagnosed between 20 and 50 years of age, with mean age of diagnosis of malignancy of 31 years. These are mostly chondrosarcomas and most often arise in the pelvis. Excision can be curative since chondrosarcomas tend to be slow to metastasize.

MONITORING: Patients should be taught body awareness and should report any change in size of known and palpable exostoses that arises after reaching maturity. Skeletal survey to document sites of exostoses should be completed in late adolescence. With any suspicion of change in size (or onset of new pain) then that area should be assessed radiographically. Scintigraphic bone scan can be used for screening (high false positive rate but low or nonexistent false negative rate). If bone scan is positive or plain radiographs show worrisome features, these should be followed by magnetic resonance imaging of the area of concern. If MRI is positive or suspicious then excisional biopsy is indicated.

INTERVENTION: Excision if malignancy is demonstrated. These are usually low grade, slow growing malignancies and primary excision is usually successful.

PROBLEM: GENERALIZED PAIN

EXPECTATIONS: Exostoses may be painful for a number of different reasons (discussed above). In addition, however, many individuals with this disorder report generalized pain of undetermined origin

MONITORING: Pain assessment should be part of management of individuals with Multiple Exostoses.

INTERVENTION: Usual modalities of pain management, including involvement of pain specialists, should be employed as needed.

PROBLEM: FOREARM DEFORMITY

EXPECTATIONS: Progressive changes of the forearm, with bowing, disproportionate shortness of the ulna and consequent ulnar deviation of the hand occur in 40-70% of affected individuals, beginning in mid-childhood. In about 20% frank radial head dislocation will occur. Function usually remains adequate although loss of pronation-supination is usual in the affected subgroup. Radiocarpal subluxation may also occur.

MONITORING: By periodic clinical assessment.

INTERVENTION: Various treatment options have been suggested for radial head dislocation – radial head resection, radial shortening, radioulnar fusion etc. Of the options available ulnar lengthening using an external distracter seems to have had the best overall outcomes. However, many individuals will choose not to have surgery, and function in adulthood of those choosing this course is only modestly affected.

PROBLEM: HAND INVOLVEMENT

EXPECTATIONS: Around 50-70% have some hand involvement. Most often exostoses affect the metacarpals and proximal phalanges. Moderate disproportionate shortening is common. Angular deformity of the fingers may arise, perhaps in 10-15%. Nailbed involvement can result in longitudinal ridging of the nails

MONITORING: By periodic clinical assessment.

INTERVENTION: Wedge osteotomy surgery may be indicated if angular deformity is marked.

PROBLEM: LEG LENGTH DISCREPANCY

EXPECTATIONS: Probably around ½ of all affected individuals will develop a leg length difference during childhood, usually of modest severity.

MONITORING: Specific clinical assessment should occur every 1-2 years during childhood. If significant discrepancy is detected, then scanogram radiographs may be needed to chart the rate of increase of the discrepancy. Low back pain is the most common symptom related to a leg length difference.

INTERVENTION: Depending on severity, treatment may be: a. none; b. internal or external shoe lift; c. timed epiphysiodesis of the distal femoral and/or proximal tibial epiphyses in the longer leg; d. leg lengthening.

PROBLEM: LEG POSITION ABNORMALITIES

EXPECTATIONS: Valgus deformity at the knees is the most common (5-25%). Ankle valgus deformity is also relatively common. These arise secondary to fibular exostoses and consequent fibular shortening.

MONITORING: Specific clinical assessment should occur every 1-2 years during childhood. If knee valgus exceeds around 20° or is seriously symptomatic, then surgical correction may be indicated.

INTERVENTION: Varus osteotomy surgery is most often used. Other alternatives that might be considered include hemiepiphyseal stapling, 8-plates, etc.

PROBLEM: PELVIC EXOSTOSES IN FEMALES

EXPECTATIONS: Women, on reaching reproductive age, may have pelvic exostoses that can interfere with delivery. About 60% of women with this disorder deliver by cesarean section.

MONITORING: Assess initially at time of skeletal survey in late adolescence. Insure that obstetrician is aware of this potential complication.

INTERVENTION: Cesarean section if warranted.

GENETICS AND MOLECULAR BIOLOGY

Multiple Exostoses is caused by an autosomal dominant gene abnormality. This means that an adult with this disorder will have a 50% chance to pass this poorly functional gene on to each child. About one-third of individuals with this disorder will be born to unaffected parents. This arises because of a new chance change (mutation) in only the single egg or single sperm giving rise to the affected individual.

The gene changes resulting in Multiple Exostoses are fully penetrant (that is, anyone with the gene change has at least mild manifestations of the disease) but markedly variable in expression. Severity may be, on average, greater in males than in females.

Most individuals will have a causal change in one of two genes, *EXT1* (around 60%) or *EXT2* (around 25%). There are additional mapped loci that are not well characterized. It appears that in virtually every regard those with *EXT1* mutation have, on average, more severe problems – more exostoses, more secondary complications, more frequent malignant transformation. However, the overlap in severity for all of these is sufficiently great that differences in monitoring based on which gene is involved are not justified.