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

NAIL-PATELLA SYNDROME
NATURAL HISTORY

INTRODUCTION:

The following summary of the medical expectations in Nail-Patella syndrome 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].

Nail-Patella syndrome is an infrequent disorder, thought to affect around 1 in 100,000 individuals. As its name implies, two of its primary features are abnormalities of the nails and of the patellae. Nail involvement is present in 98% of those diagnosed, while patellar abnormalities affect around 90%. In addition, iliac horns (which are usually diagnosed radiologically but which sometimes are clinically evident) and abnormality of elbow mobility affect 80% or more of individuals with Nail-Patella syndrome.

MEDICAL ISSUES TO BE ANTICIPATED

PROBLEM**: NAIL DYSTROPHY**
EXPECTATIONS: Virtually all affected individuals have dystrophic nails. The radial (thumb side) nails tend to be more severely involved, and the hands are more often more severely affected than the feet. This feature is non-progressive
MONITORING: -
INTERVENTION: This is usually only of cosmetic consequence. No medical implications are present.

PROBLEM**: PATELLAR ABNORMALITIES**
EXPECTATIONS: Most often the patellae are either absent or markedly hypoplastic. Consequences can vary from no clinical effect to issues related to poor tracking, instability and giving way, chronic pain, etc.
MONITORING: Historical and clinical assessment of knee function.

INTERVENTION: Although this usually requires no treatment, occasionally either patellar realignment surgery or patellectomy is needed.

PROBLEM**: ELBOW ABNORMALITIES**
EXPECTATIONS: Limited elbow mobility is present in 70-90% of affected individuals. It is non-progressive. However, some have radial head dislocation.
MONITORING: Clinical assessment of elbow mobility and inquiry regarding elbow pain.
INTERVENTION: Limited movement with radial head dislocation requires no intervention. Rarely surgery is indicated in those with radial head dislocation – because of intractable pain or marked progression of limitation of movement. Surgery may include head excision or osteotomy surgery.

PROBLEM**: FOOT AND ANKLE**
EXPECTATIONS: Around 20% are born with clubfeet, most often with equinus deformity. In addition, even in those without frank clubfoot, tight heel cords with toe walking are more common.
MONITORING: Assessment in infancy.
INTERVENTION: The usual interventions for clubfeet are effective when this is present.

PROBLEM**: OTHER ORTHOPEDIC COMPLICATIONS**
EXPECTATIONS: A large number of other orthopedic features are sometimes present, including the following – back pain is present in ~50% of adults, without understood cause; scoliosis arises in ~20% but is usually modest and most often doesn't require treatment. Less frequent or less relevant characteristics may include pectus excavatum, decreased development of the upper arms, structural abnormalities of the shoulder girdle, instability of metacarpophalangeal joints and proximal interphalangeal joints, spondylolysis, leg length discrepancy, hip abnormalities, knee flexion contractures, valgus deformity at the knees.
MONITORING: Historical and clinical assessment yearly during childhood.
INTERVENTION: Most require no treatment. All others should be managed as they would be in an individual without the underlying diagnosis of Nail-Patella syndrome.

PROBLEM**: OSTEOARTHRITIS**
EXPECTATIONS: Premature development of osteoarthritis seems to be very common in adults with Nail-Patella syndrome.
MONITORING: Historical and clinical assessment, and radiographs as indicated.
INTERVENTION: Modest limitations to decrease risk factors for osteoarthritis might be appropriate in childhood and in young adults, such as limitation of repetitive weight-bearing and avoidance of collision sports.

PROBLEM**: RENAL INVOLVEMENT**
EXPECTATIONS: *This is the most important and sometimes overlooked health issue in those with Nail-Patella syndrome.* Various population based studies have estimated that kidney abnormality

is present in between 30% and 58% of individuals with this disorder. Usual first presentation is proteinuria with or without hematuria. It is most often benign and non-progressive. *However*, in a minority it will progress and lead to renal failure – estimates ranging from 3% to 30%, with most studies showing frequencies clustering around 10%-20% of those with Nail-Patella syndrome. The mean age of renal failure in those in whom it develops is ~33 years. (There also is a higher frequency of preeclampsia in pregnancy.)
MONITORING: Urinalysis, creatinine clearance and quantitative urine protein at initial diagnosis and then yearly. Blood pressure measurement should be done at every health care contact.
INTERVENTION: Referral for aid in management to a nephrologist. Hypertension management is not different than in others with renal hypertension. Renal transplantation is successful when needed.

PROBLEM**: GLAUCOMA**
EXPECTATIONS: Primary, open angle glaucoma arises in 10%-20% of affected individuals. Mean age of detection is 46 years, but it may be present much earlier, appearing sometimes in childhood.
MONITORING: Ophthalmologic assessment, including tonometry, at initial diagnosis and then every 1 to 2 years.
INTERVENTION: Management is the same as those with glaucoma from other causes.

PROBLEM**: OTHER**
EXPECTATIONS: A host of other complications have been reported at an incidence higher than in the general population including irritable bowel, chronic constipation, peripheral neuropathy, poor peripheral circulation, Raynaud syndrome, and, perhaps, seizures, and ADD/ADHD.

GENETICS AND MOLECULAR BIOLOGY

Nail-Patella syndrome is uniformly caused by an autosomal dominant, single gene abnormality. This means that an adult with this disorder will have a 50% chance to pass the poorly functional gene on to each child. Infrequently an individual with this disorder will be born to unaffected parents because of a new chance change (new mutation); never is the poorly functional gene 'hidden' and, so, in this circumstance the parents have virtually no risk that additional children will be similarly affected. However there is marked variability of effects even within affected members of the same family.

This disorder is usually (perhaps always) the result of a change in the *LMX1B* gene. While molecular testing is possible, it is rarely necessary since clinical diagnosis is usually straightforward.