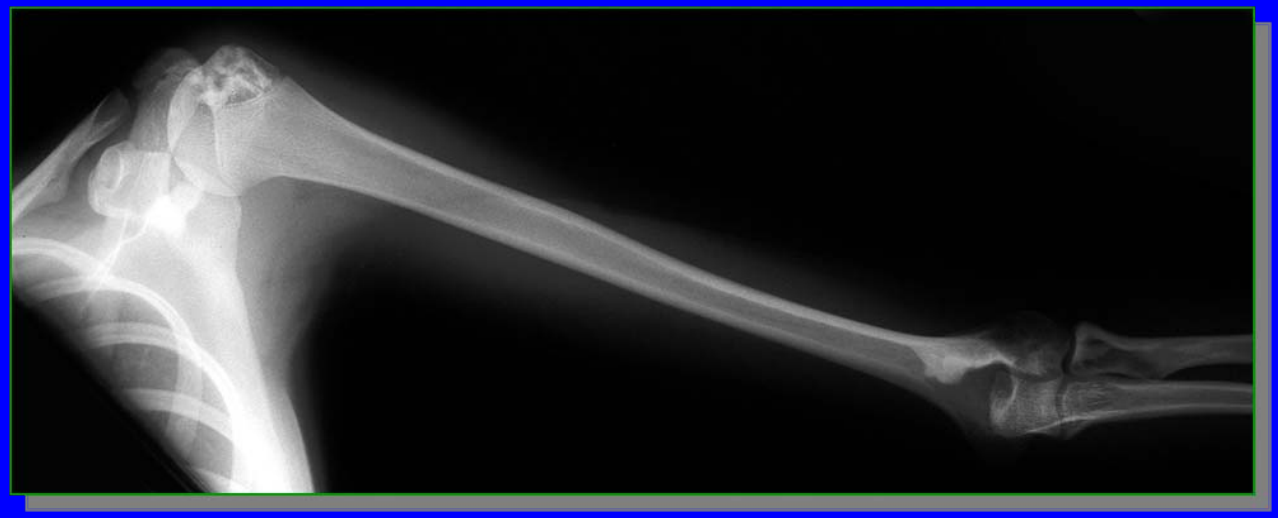
Melorheostosis

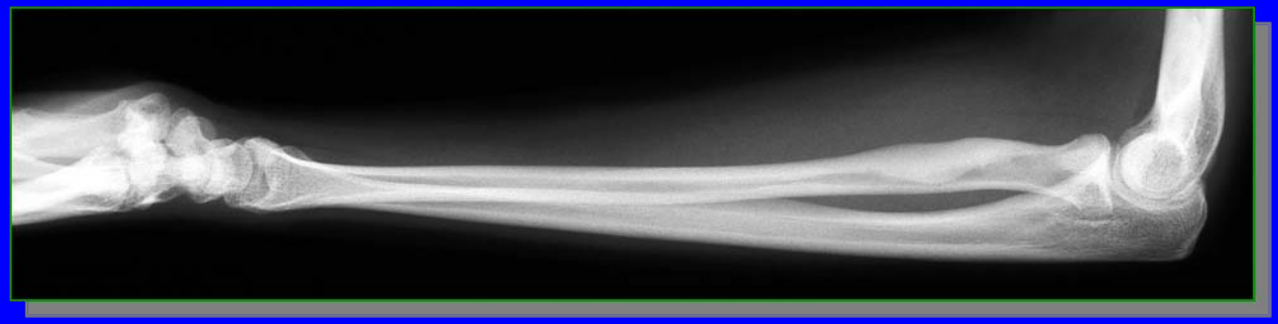
Deborah Wenkert, M.D.

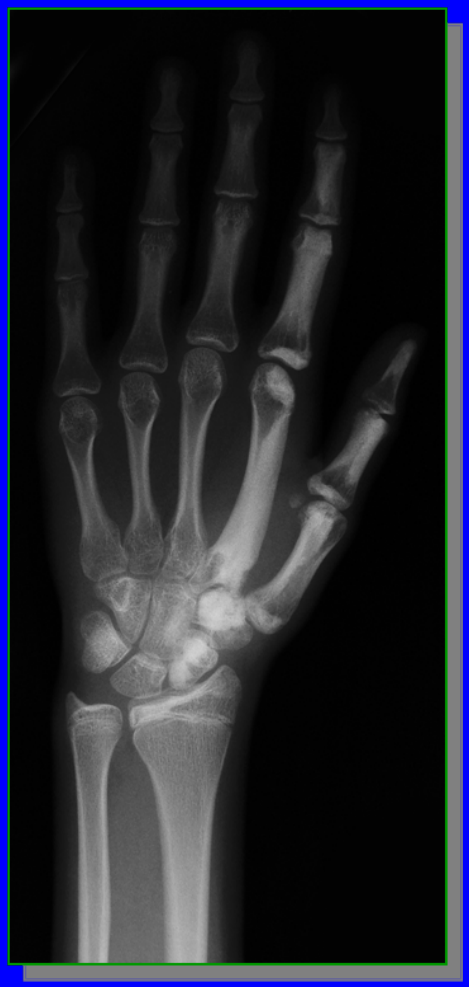
Center for Metabolic Bone Disease and Molecular Research,
Shriners Hospital for Children;
St. Louis, Missouri, U.S.A.

What is Melorheostosis? (OMIM 155950)

A rare form of hyperostosis characterized by its linear pattern of distribution along the major axis of long bones. Named for the Greek words melos (member) and rhein (flow).







Features of Melorheostosis

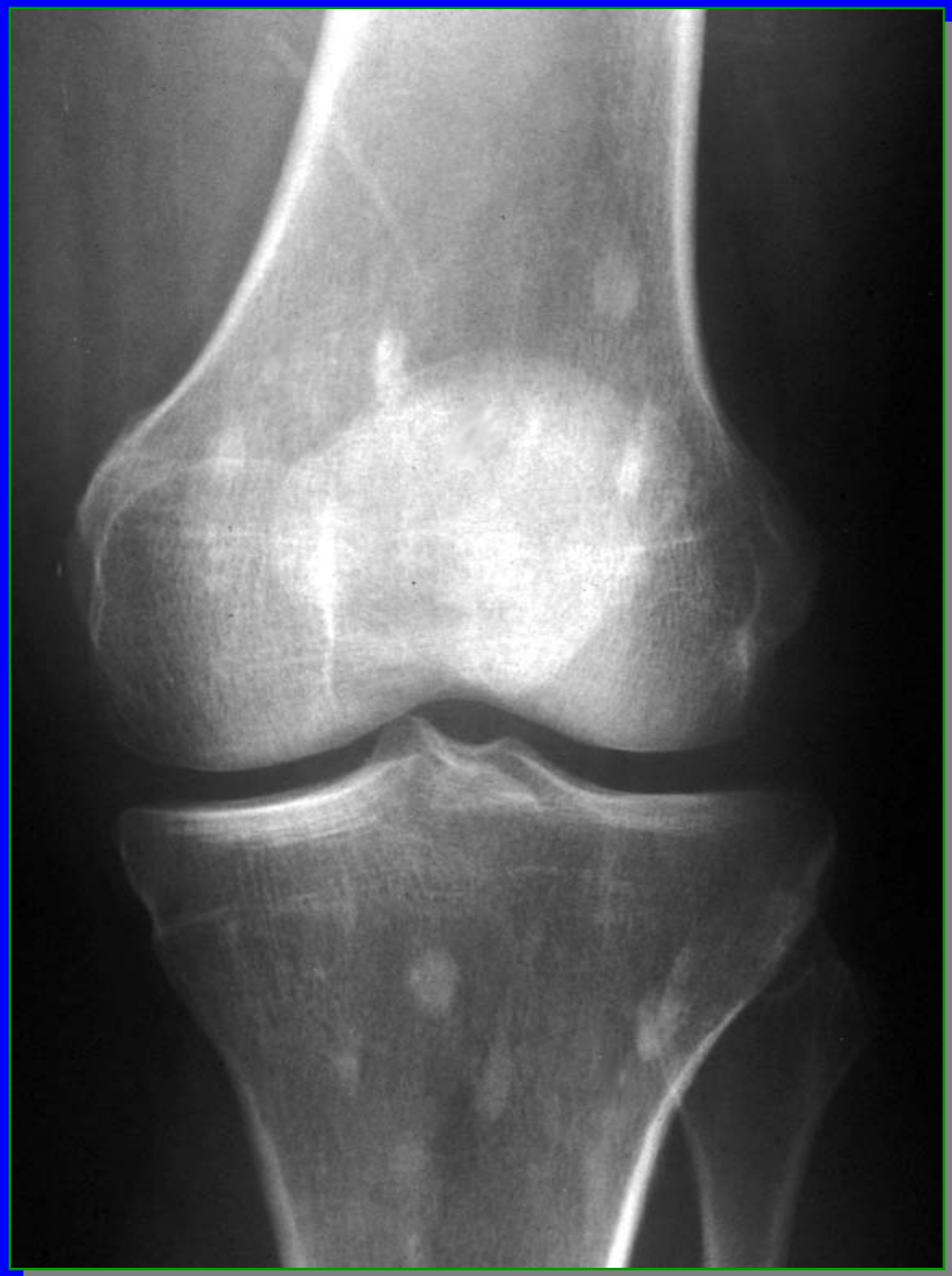
Gamut Index of Skeletal Dysplasias, 2nd ed

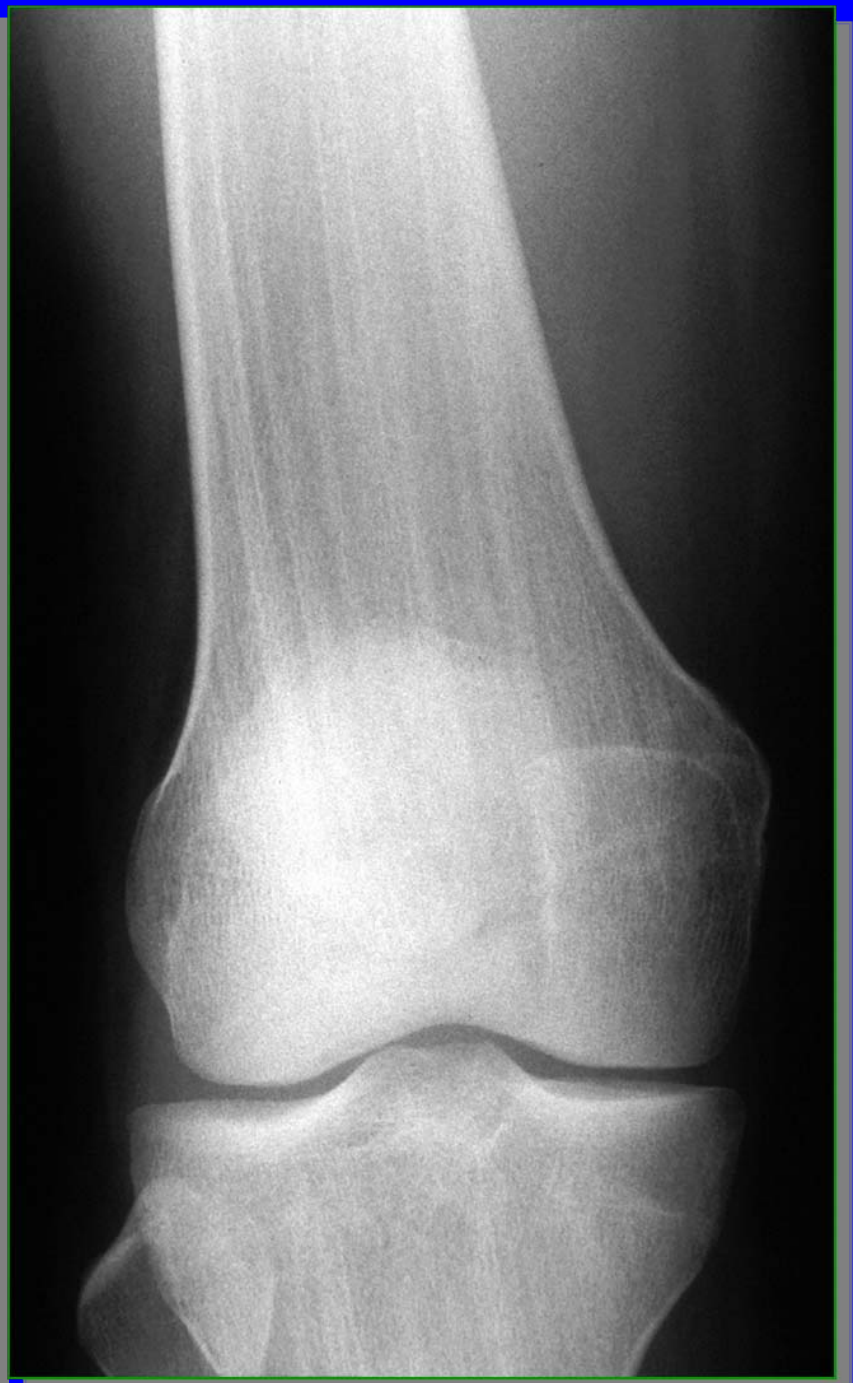
- Clinical: Asymptomatic or localized pain with sclerotic dermal changes and joint contractures
- Radiographic: Unilateral, irregular, linear areas of increased density which appear to be flowing down the long axes of the tubular bones
- Genetics: Non-genetic

MEL as a feature of other diseases:

- **Osteopoikilosis/Buschke-Ollendorff Syndrome (*LEMD3* inactivating mutations)**
- **Mixed Sclerosing Bone Dystrophy**
- **MEL with Minimal Change Nephrotic Syndrome, Mesenteric Fibromatosis, and Capillary Hemangiomas**
- **MEL & tricho-dento-osseous syndrome**
- **MEL involving the Craniofacial Skeleton**
- **MEL of the Axial Skeleton with Associated Fibrolipomatous Lesions**

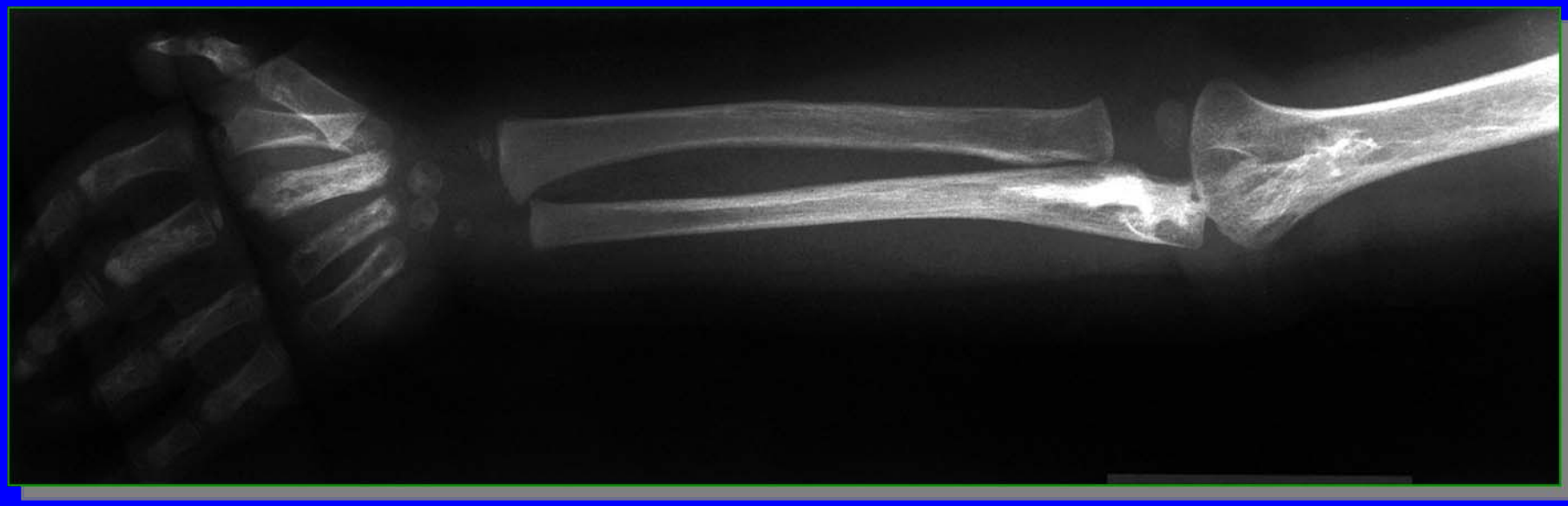
vs. Classic Melorheostosis (MEL)





Classic Melorheostosis

- Girl: Gestation complicated by gastrointestinal bacterial infection treated with IV antibiotics.
- Age 4 months – ulnar deviation of her right wrist. Holds left thumb in palm.
- Age 19 months – flexion contractures of MP joints, ulna deviation of the middle phalanx, flexion contraction of PIP joint, and rotational and radial deviation deformity of the right middle phalanx, and flexion contracture of right elbow.
- **Parents' skeletal x-rays unremarkable**



Skeletal Radiol. 1979 Jun 6;4(2):57-71.

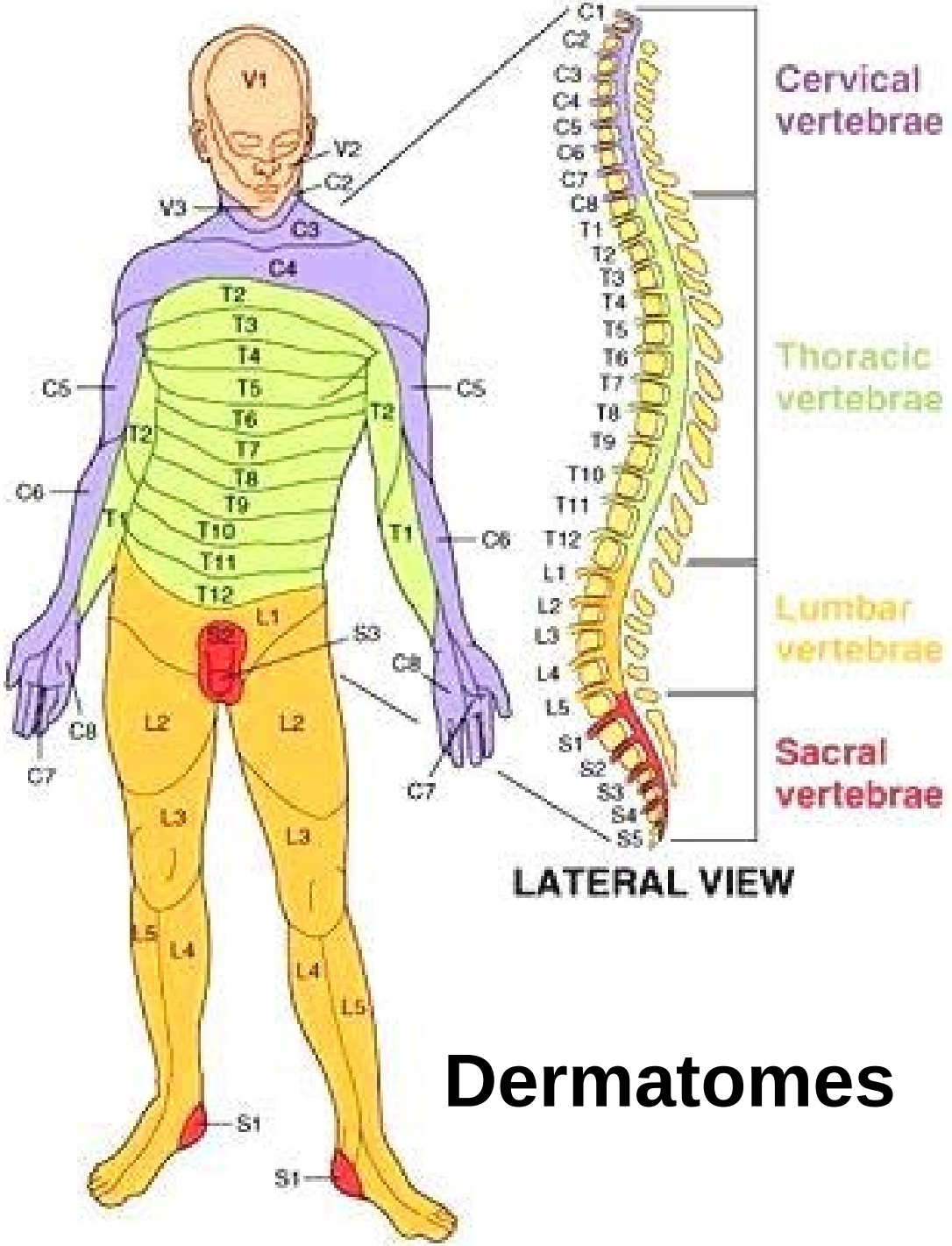
Melorheostosis and the sclerotomes: a radiological correlation.

Murray RO, McCredie J

sclerotome

an area of bone innervated by a single spinal nerve and its branches.

During somite maturation, the ventral half of the epithelial somite disintegrates into the mesenchymal sclerotome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S3
S4
S5
Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
Sacral vertebrae
LATERAL VIEW
Dermatomes

Pathogenesis?

Hypotheses have included:

- Reaction to infection
- Reaction to trauma
- Sensory neuropathy
- Vascular abnormality
- Autoimmune disease
- Post zygotic mutation

Is the pathogenesis of ‘Classic Sporadic Melorheostosis’ different from that of MEL when it occurs in less common locations (craniofacial or axial skeleton) or as a feature of another disease?

Until the cause of sporadic melorheostosis is known, choosing a subset may help define the pathogenesis.

324 pubmed results for melorheostosis

Melorheostosis

Campbell et al, J Bone Joint Surg Am. **1968** ;50:1281-1304

- Contractures, fibrosis and abnormal skin
- Present from birth or early childhood
- Bone changes may not appear for several years
- Hyperostosis progresses
- The skull, spine, and ribs are least commonly affected.
- Monostotic, polyostotic or monomelic and more rarely: multiple limbs and the trunk.
- Limb length discrepancy
- Abnormal circumference and/or contours

Melorheostosis Association website

- The Melorheostosis Association hosts a website on which 174 people with melorheostosis have posted their medical histories.


Edit View History Bookmarks Tools Help
http://www.melorheostosis.com/default.htm
melorheostosis association
Getting Started Latest Headlines Customize Links Free Hotmail Windows Marketplace Windows Media Windows
http://www.melorheostosis.com
Melorheostosis ASSOCIATION
Cause Treatment cure
WELCOME
Home
Personal Histories
Add Personal History
Conferences - 2003 - 2005
2005 Conference Papers
2006 Conference Papers
Brochure
WHO ARE WE?
The Melorheostosis Association is a not-for-profit organization dedicated to finding the cause, treatments and cure for melorheostosis. Our focus is on promoting greater awareness and understanding of this progressive disease and its manifestations through education, research, communication and advocacy efforts on behalf of those affected by it as well as those dedicated to alleviating it. For a full list of our Board of Directors, click here.
Our world renowned Scientific and Medical Advisory Panel is led by Dr. Frederick Kaplan, Chief of the Division of Metabolic Bone Diseases and Molecular Medicine at the University of Pennsylvania. For a full list of the Medical Panel, Click here
Melorheostosis.org is:
-- the largest database of melorheostosis patients in the world
-- a community of melorheostosis patients and their families joined to
WHAT IS MELORHEOSTOSIS?
Melorheostosis is a rare and progressive disorder characterized by hyperostosis (thickening) of the cortical bone. Melorheostosis affects both bone and soft tissue growth and development. Melorheostosis can result in severe functional limitation, extensive pain, soft tissue contractures, and limb, hand an/or foot deformity. The age of diagnosis is typically based on the severity of onset and symptoms. On x-rays, the appearance of melorheostosis been likened to flowing, melted candle wax.
Diseases associated with melorheostosis include, osteopoikilosis, osteopathia striata, scleroderma and Buschke-Ollendorff syndrome.
Note: for additional information, please see the "buttons" on the left, including "Research Links" and "Brochure."
Melorheostosis.org is:
-- the largest database of melorheostosis patients in the world

‘Personal history’ analysis from the Melorheostosis Association website

Advantages:

No page limitations (more clinical information than some papers)

Large number of patients

Negative results are available

Disadvantages:

Accuracy

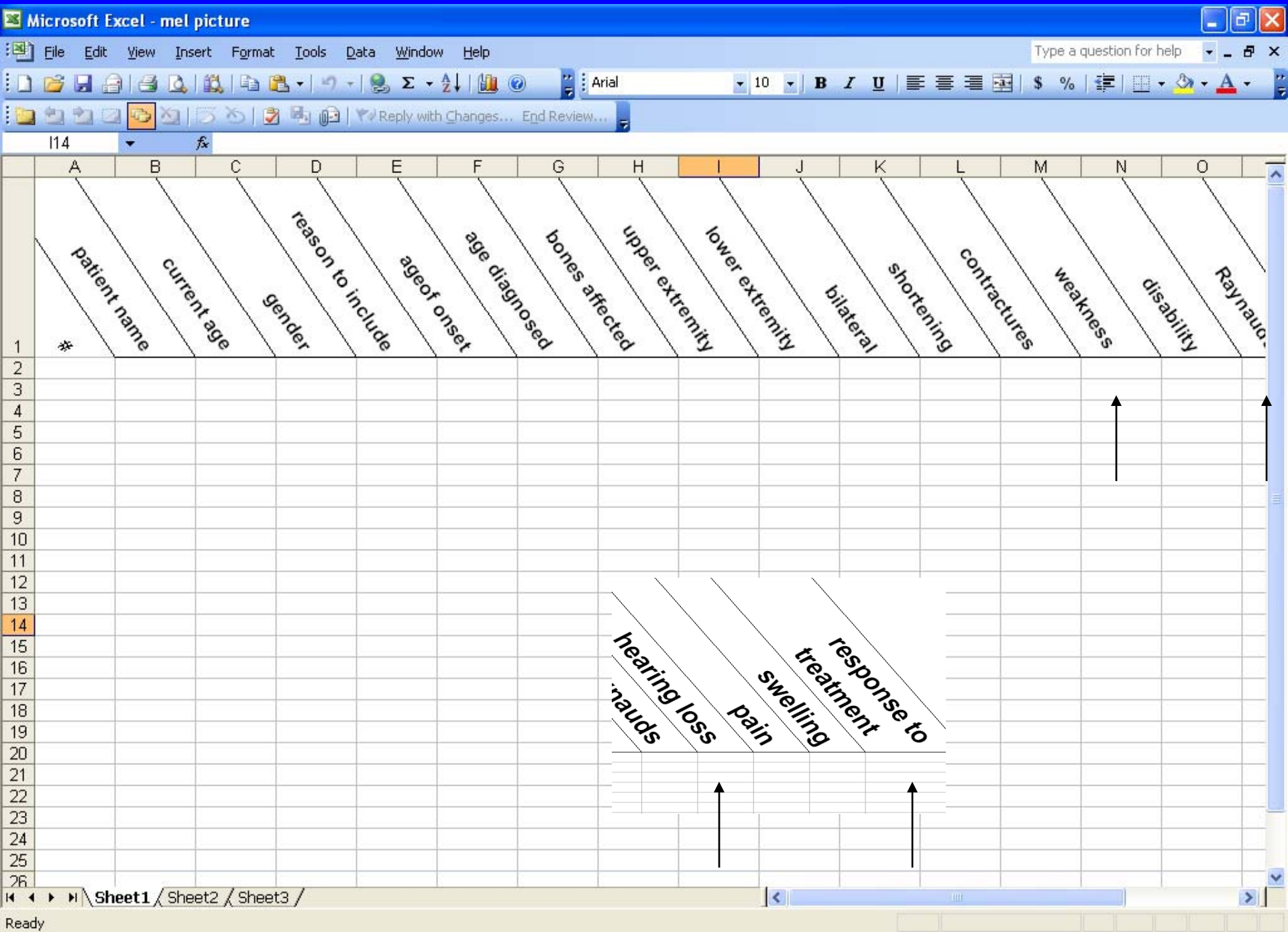
no radiographs

duplicating the literature

ascertainment bias (pain, function, age, sex)

A review of histories posted before 8/27/2008, yielded 121 nonfamilial, nonaxial cases:

- 2.6 X more women than men.
- Most (80) were under 40 yrs of age,
- 24 of whom were children.
- Age of onset in childhood was twice as common as adulthood (69:34) ranging from onset at birth (8) to 40’s.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bilateral
shortening
contractures
weakness
disability
Raynaud
response to treatment
swelling
pain
hearing loss
Sheet1 Sheet2 Sheet3
Ready

Of 121 *nonfamilial nonaxial* cases of Melorheostosis posted on the website:

Laterality: 6 bilateral, 98 unilateral

Extremity: 77 leg(s), 37 arm(s), 6 both

Pain: 93 painful, 16 nonpainful

Limb shortening: 17

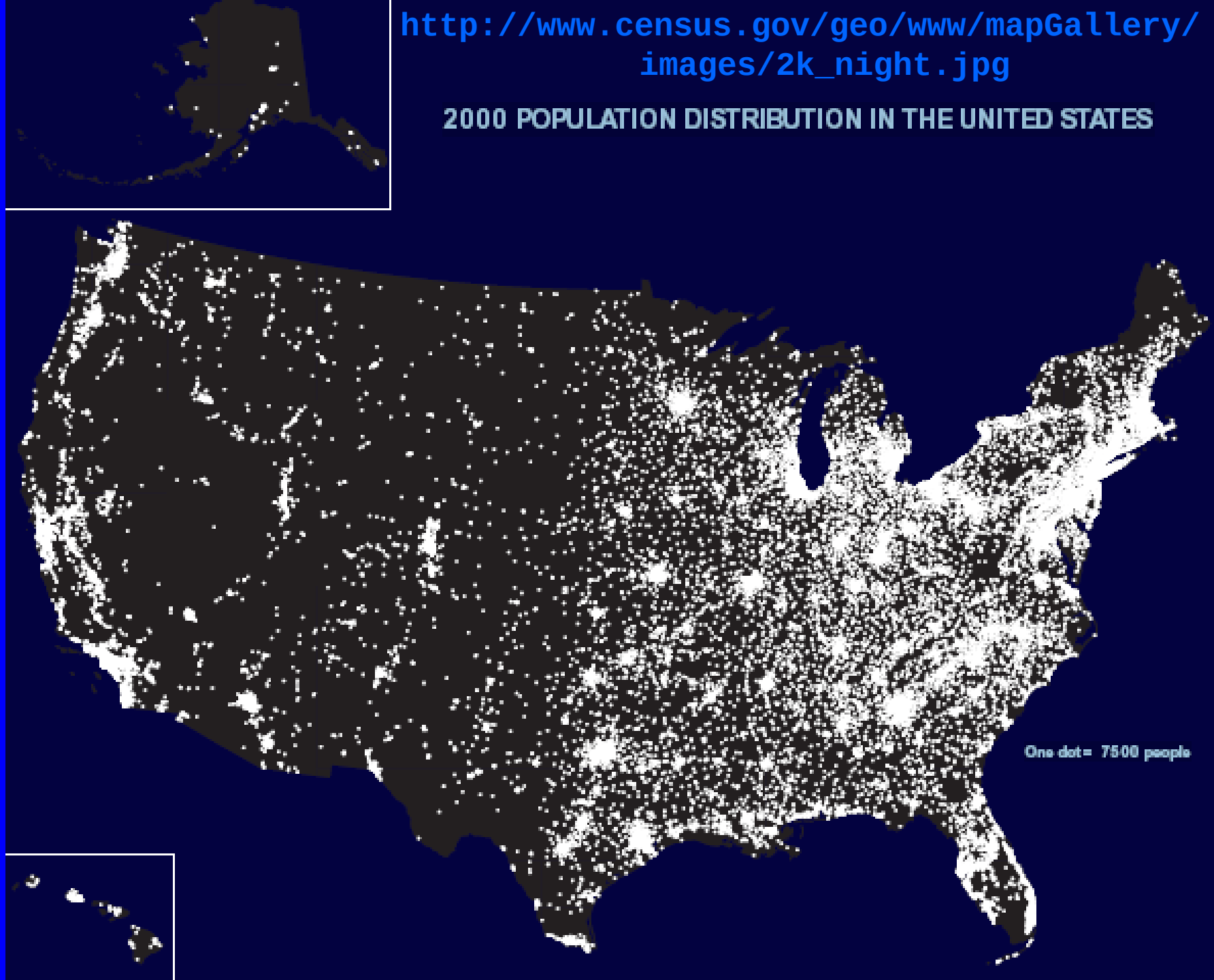
Decreased range of motion: 37

Swelling: 14

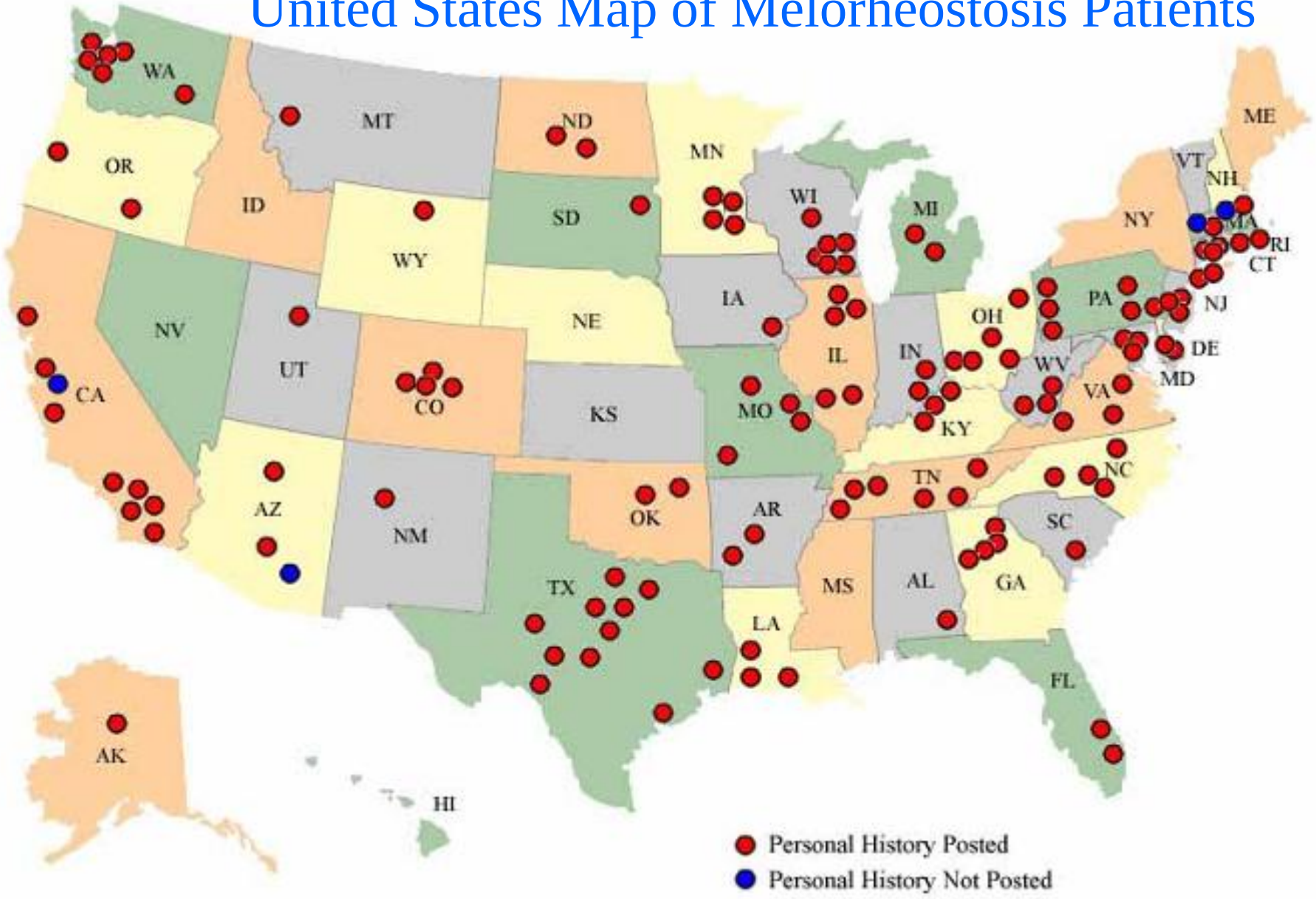
Raynaud's: 1

Geographic Distribution?

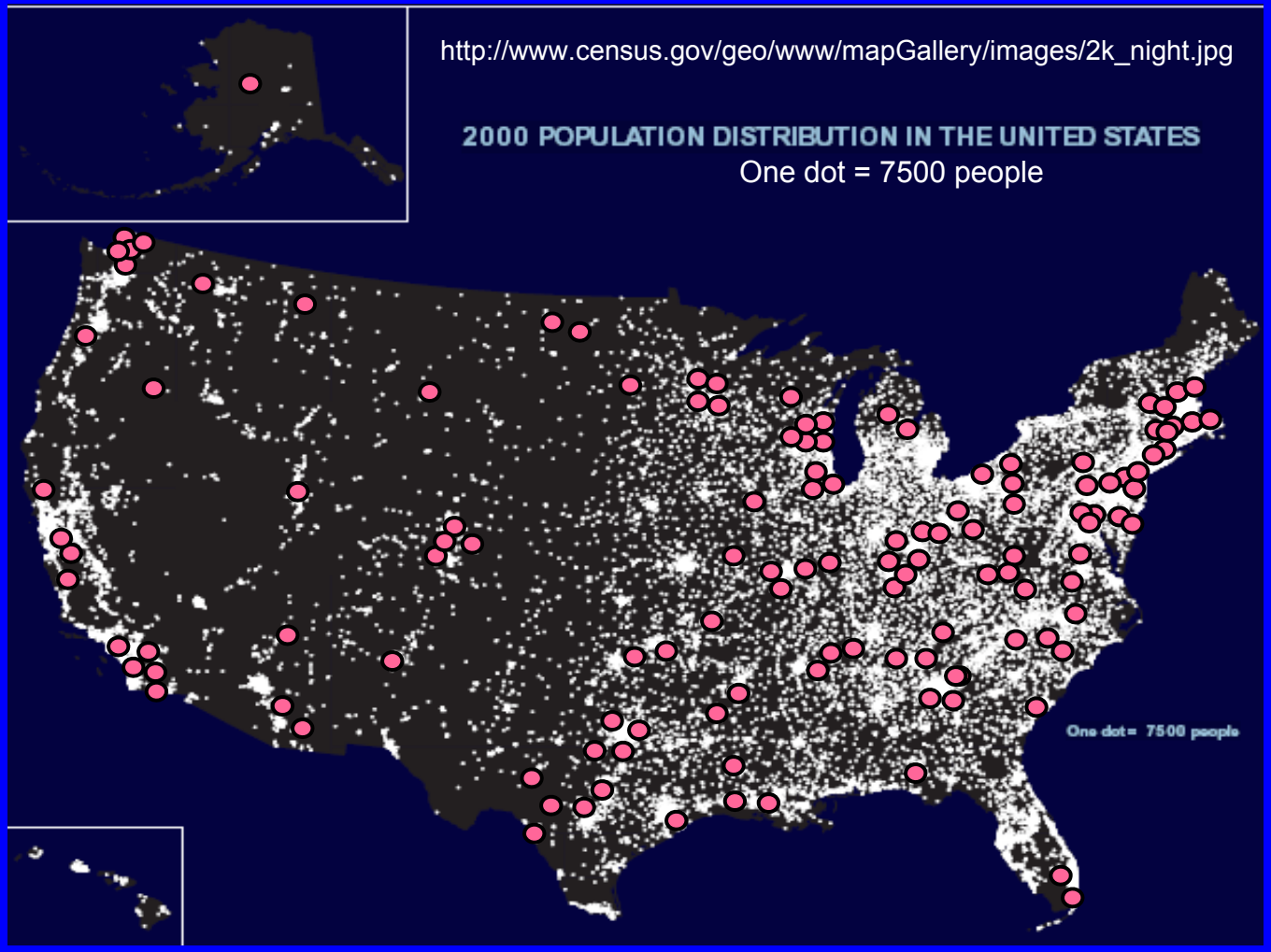
http://www.census.gov/geo/www/mapGallery/images/2k_night.jpg



United States Map of Melorheostosis Patients



http://www.melorheostosis.com/default_files/Page1000.htm



● Melorheostosis Patients

http://www.melorheostosis.com/default_files/Page1000.htm

Perhaps this makes infectious and toxic exposures less likely.

Mosaicism instead of infection of sensory nerve

Eur. Radiol. (2001) 11: 474–479

MUSCULOSKELETAL

J. Freyschmidt

Melorheostosis: a review of 23 cases

Received: 2 March 2000
Revised: 1 June 2000

Abstract The aim of this study was to review clinical and radiological wax appearance ($n = 5$); myositis ossificans-like ($n = 1$); osteopathia

Suggestions of neonatal onset:

- Even though some present in adulthood, positive bone scan and pain can predate the radiographic appearance.
- No reports of phantom limb pain or sensation. PLEASE NOTE: I HEARD AFTER THE LECTURE THAT THIS HAS OCCURRED!
- However, although many patients have abnormalities at birth, most of the skeletal disturbance appears later without reports of prenatal ultrasound skeletal dysplasia

Early onset, developmental patterning of bone abnormalities, and lack of inheritance may argue for somatic mosaicism of any number of genes that condition bone formation and mass (or for an *in utero* toxin or infection)

Are genes differentially expressed between the normal and involved skin in MEL?

J Cell Biochem. 2000 Mar;77(2):169-78.

Kim JE, Kim EH, Han EH, Park RW, Park IH, Jun SH, Kim JC, Young MF, Kim IS

A TGF-beta-inducible cell adhesion molecule, betaig-h3, is downregulated in melorheostosis and involved in osteogenesis.

Br J Dermatol. 2003 Apr;148(4):799-803.

Increased procollagen alpha1(I) mRNA expression by dermal fibroblasts in melorheostosis.

Endo H, Katsumi A, Kuroda K, Utani A, Moriya H, Shinkai H.

There is much work left to be done to address the pathogenesis and treatment of melorheostosis

Thank-you to
The patients on the Melorheostosis web site
Nurses and staff at the research center

Michael P Whyte, MD
William H McAlister, MD

Thank You

J Wildl Dis. 1985 Oct;21(4):386-90.
Davidson WR, Nettles VF, Couvillion CE, Howerth EW

Diseases diagnosed in wild turkeys (Meleagris gallopavo) of the southeastern United States.

Histology: cortical sclerosis partially obliterating the medullary cavity. Small haversian systems wide band of parallel lamellae along the endosteal surface. In all bones examined. Some areas of less mature bone with active bone turnover and enlarged haversian canals. Round nodules of lamellar bone in the ends of the short tubular bones. And in the epiphyseal regions of the long bones. Some of the nodules contained radiating spicules. Focal areas of prominent periosteal bone formation were seen in both long and short tubular bones. Focal osteoarthritis was seen in the knee ankle and interphalangeal joints. No cartilaginous tissue or necrotic bone no projections over the cortex and no soft tissue ossification. Soft tissues around the ankle and knee had extensive fibrosis with focal proliferation of small capillary vessels.

- limb length discrepancy, deformity or joint contractures which may be seen before radiographic evidence of MEL
- 4 from antiquity, 3 follow-up>19 years
- Vascular abnormalities
- Osteosarcoma (3)

- Lifestyle impact: exercise, diet, weight
- Is the increased incidence in women real?
- Nerve distribution: clue to therapy-nerve block
- Prevalence of other problems (Raynauds, MRA’s or surgical or autopsy results)

Deactivating Germline mutations in LEMD3 Cause Osteopoikolosis and Buschke-Ollendorf Syndrome, But Not Sporadic Melorheostosis

Mumm S, Wenkert D, Zhang X, McAlister, WH, Mier R, Whyte MP JBMR 22:243-250, 2006

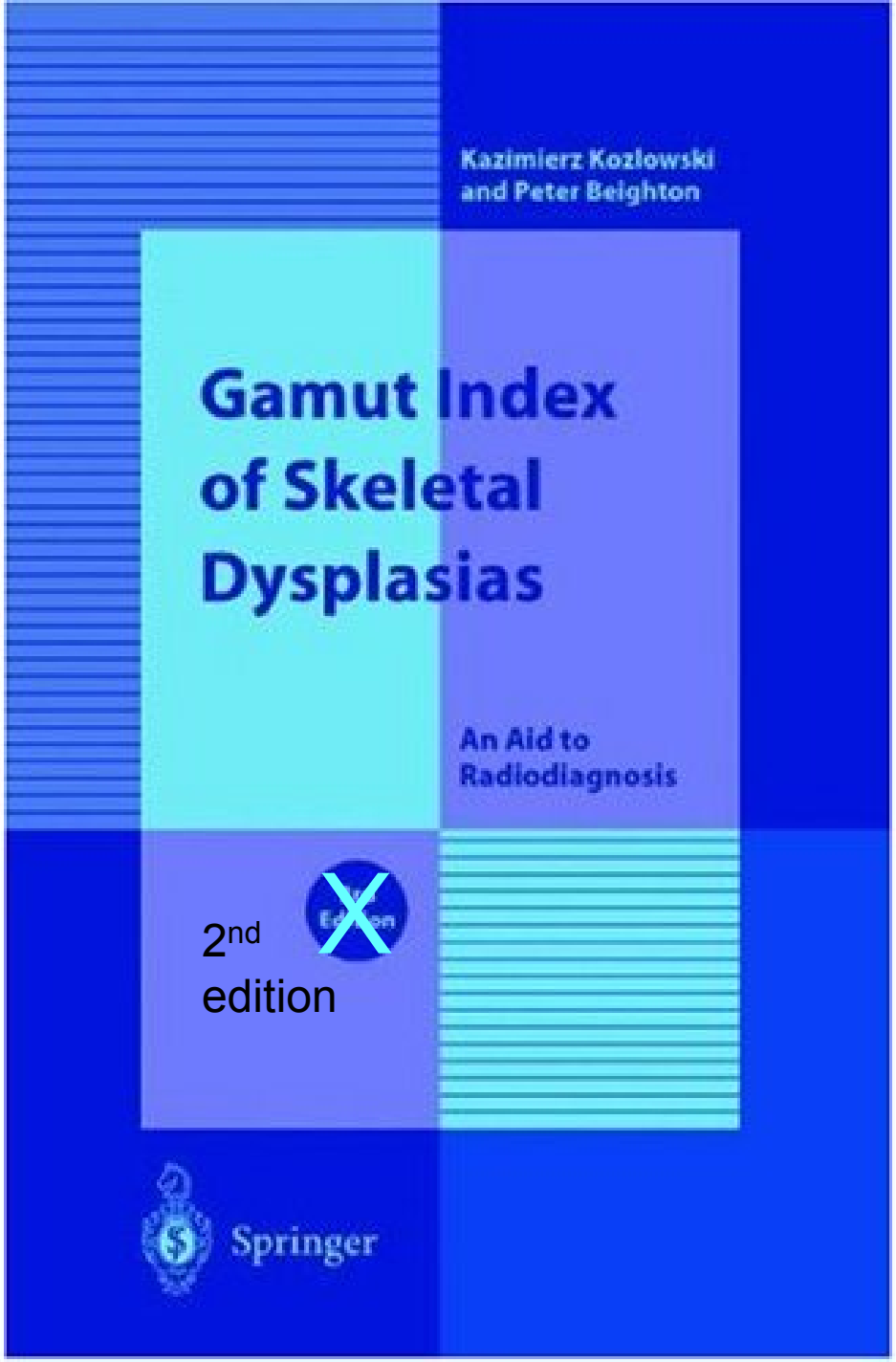
60-80% of amputees experience phantom pain Phantom pain is less common in congenital cases

- Bone. 2005 Feb;36(2):232-42.
-
  Beta ig-h3 mediates osteoblast adhesion and inhibits differentiation.

  Thapa N, Kang KB, Kim IS.

Classic Melorheostosis

- 16 year old Caucasian girl
- Age 7 – unable to extend left thumb
- Age 13 – painful hand cramps. X-ray = MEL in the first and second phalanges and radial carpal bones
- **Skin tight** over abnormalities of left hand
- No family history of MEL
- **Family x-rays unremarkable**


Kazimierz Kozlowski
and Peter Beighton
Gamut Index
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Dysplasias
An Aid to
Radiodiagnosis
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