UCONN SCHOOL OF MEDICINE

Connecticut Children's MEDICAL CENTER

RARE BONE DISORDERS:
Helping through clinical care & research

Emily L. Germain-Lee, M.D.
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From Bedside . . .

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. . . to Bench . . .

And

Back Again

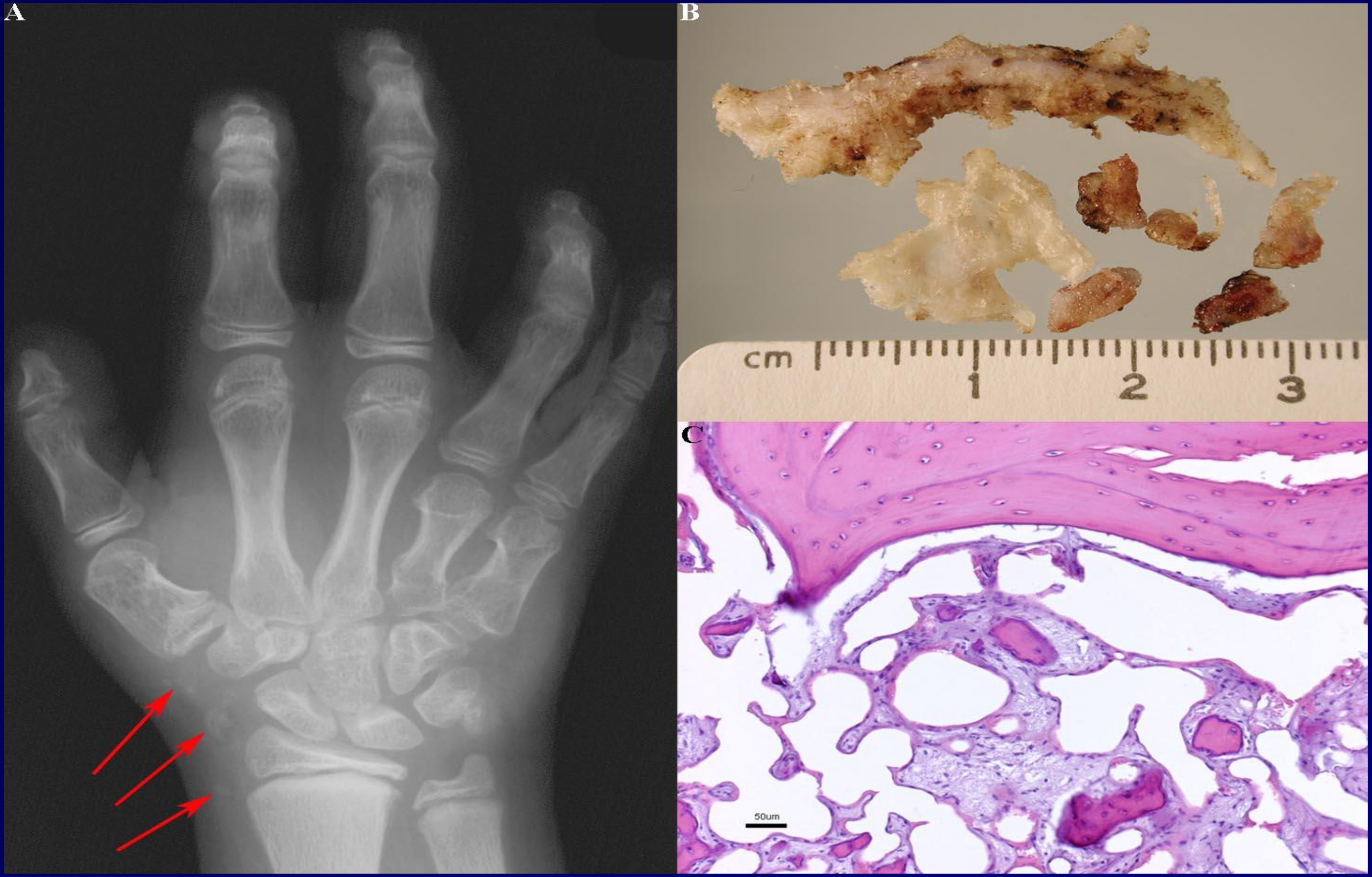
Albright Hereditary Osteodystrophy (AHO)

- Follow largest population of patients worldwide
- Devastating condition due to mutations in a gene necessary for many important hormones to act
- Patients have problems with growth, metabolism, bone formation, and calcium regulation – even with cognition
- Calcium can drop to dangerously low levels → seizures and death can occur

Albright Hereditary Osteodystrophy

Heterotopic Ossifications in AHO

Bone forms spontaneously -- painful

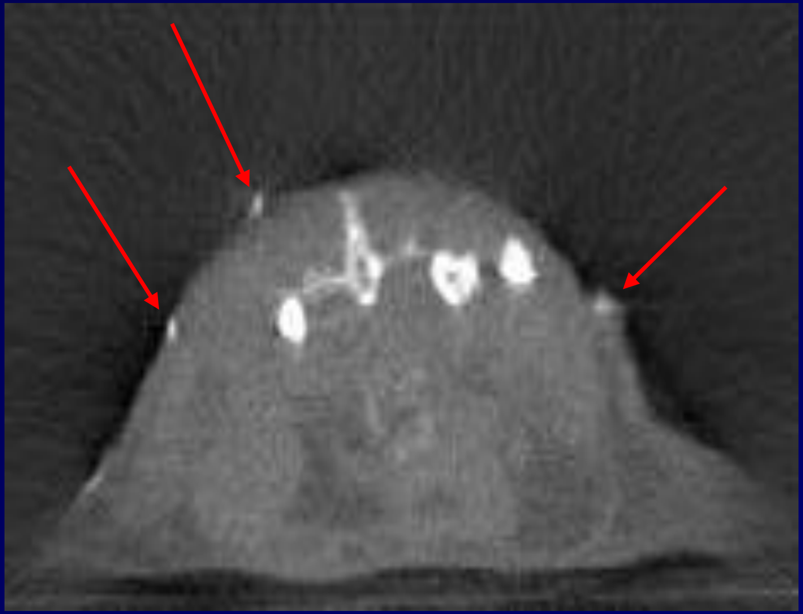


Generated Mouse Model of AHO that Recapitulates Human Disorder

Mice with AHO genetic defect provide model to examine pathogenesis and treatment

X-ray showing subcutaneous ossifications

Germain-Lee *et al.*, *Endocrinology,* 2005
Huso, Edie..Germain-Lee, *et al., PLoS One,* 2011



Albright Center

- Established “Albright Center” – 1st clinic dedicated to condition
- Follow largest population worldwide (~ 550) from 6 continents
- Physician referrals, research studies, ClinicalTrials.gov, ABC Nightline
- Elucidating disease mechanisms and developing new treatments through examination of patients as well as my genetically-engineered mouse model

Goal is to improve health and overall quality of life

Grants from NIH, FDA, foundations,
companies, philanthropy

Albright Center
at Connecticut Children's

- November, 2016 → moved Albright Center from Johns Hopkins/Kennedy Krieger Institute to Connecticut Children's and expanded
  - Prior patients from throughout USA and other countries are now coming to Connecticut
  - Since starting in CT: **NEW patients** from AR, AZ, CA, SD, WA, TX, WY, NM, NV, MN, NC, VA, FL, MA, VT, NY, NJ, MD, PA, RI, CT, Belgium, England, Tanzania, …Brazil and Finland upcoming

Statewide, National, & Global Impact

- Spreading the word about Albright Center
  - Member of international consensus panel
    - Met in France in March: decided standards for treatment worldwide (soon to be published)
  - Invited to give 2 “Meet The Expert” lectures on AHO at the 10th International Meeting of Pediatric Endocrinology
    - ~4,000 pediatric endocrinologists
    - Large audiences have led to many new referrals to CT

Osteogenesis Imperfecta
"Brittle Bone Disease"

[redacted]

[redacted]

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Osteogenesis Imperfecta (OI)

Patients and Mouse Model

- Often suffer from hundreds of fractures; extremely painful and debilitating condition; treated with bisphosphonate infusions

- Need multidisciplinary care – PT, OT, orthopedics, pulmonology, cardiology, rehab medicine, GI, neurology, etc.

- Moved prior OI clinic and **established new OI Center at CCMC**
    - Developing multidisciplinary clinic; major East Coast site
    - Developing international collaborations
    - Both clinical care AND clinical drug trials

- Approved as an official OI Center by the OI Foundation

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Center for Rare Bone Disorders

- Goals of Center for Rare Bone Disorders – improve care and develop new therapies through translational research for ALL rare bone disorders
- Critical to my mission is the search for etiologies of bone disorders for which the cause is not known -- 20%
- Laboratory located in Center for Regenerative Medicine & Skeletal Development at UConn Health – other investigators within Center also focus on bone disorders

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Spreading the Word

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- Expanding parent/patient advocacy and support groups locally, nationally, and internationally
- Advocate through long-term role as Vice President of the Human Growth Foundation (local, national, international)
- Rare Bone Disease Alliance Scientific Advisory Panel
  - International scientific alliance now includes UConn/Connecticut Children’s

Importance of Rare Disease Research Overall

- Study of rare disorders can unlock key biological mechanisms

- Not only important for specific rare disease but also important for understanding more common conditions

  - Osteoporosis
  - Fracture healing

- In the case of AHO, even has implications for:
  - Cognition
  - Behavior: Autism, ADHD, OCD
  - Obesity
  - Growth
  - Metabolism

Importance of Supporting Rare Disease Centers of Excellence

- Spill-over benefits beyond the specific rare disease center

  - Patients often require multi-disciplinary care
  - Promotes holistic, team-based approach to patient care that can be extended to other patients

- Brings national/international recognition to CT

  - “Rising tide lifts all boats”
  - Critical to recruiting world-class faculty and physicians to CT
  - Growth of patient base locally, nationally, and internationally
  - Growth of philanthropic support through more recognition

- Centers of Excellence create a culture of innovation

  - Clinical trials expand (NIH, FDA, industry)
  - Venture capital/biotech start-ups emerge

Supporting Rare Disease Research

- Challenges

  - Extremely low funding rates by NIH in general
  - Difficulty is securing NIH funding for rare diseases specifically
  - Grants from specific rare disease advocacy groups and foundations are generally small
  - Industry funding for rare disease research usually targets late stage projects

- Need to advocate for greater CT state support for rare disease research

  - Grants to support early stage research
  - Incentives to promote more collaboration between industry and academic investigators

Supporting Rare Disease Centers

- Genetics Expertise
  - Medicaid and private insurance approvals for genetic testing are currently being evaluated by people with limited expertise in rare diseases
  - Coverage of genetic testing is often denied on short-term costs saving basis with little understanding of the long-term costs in terms of patient care
  - Physicians and patients/families expend significant unnecessary effort appealing denials that should have been approved
  - Need to establish committee of expert physicians capable of making informed decisions regarding approval of genetic testing

- MORE SUPPORT FOR RARE DISEASE RESEARCH – especially early stage research
- ENCOURAGE COLLABORATION BETWEEN THE STATE AND ACADEMICS/INDUSTRY
- MORE REGULATION OF DESIGNATION OF MEDICAL DECISION-MAKERS

Kelley Amato