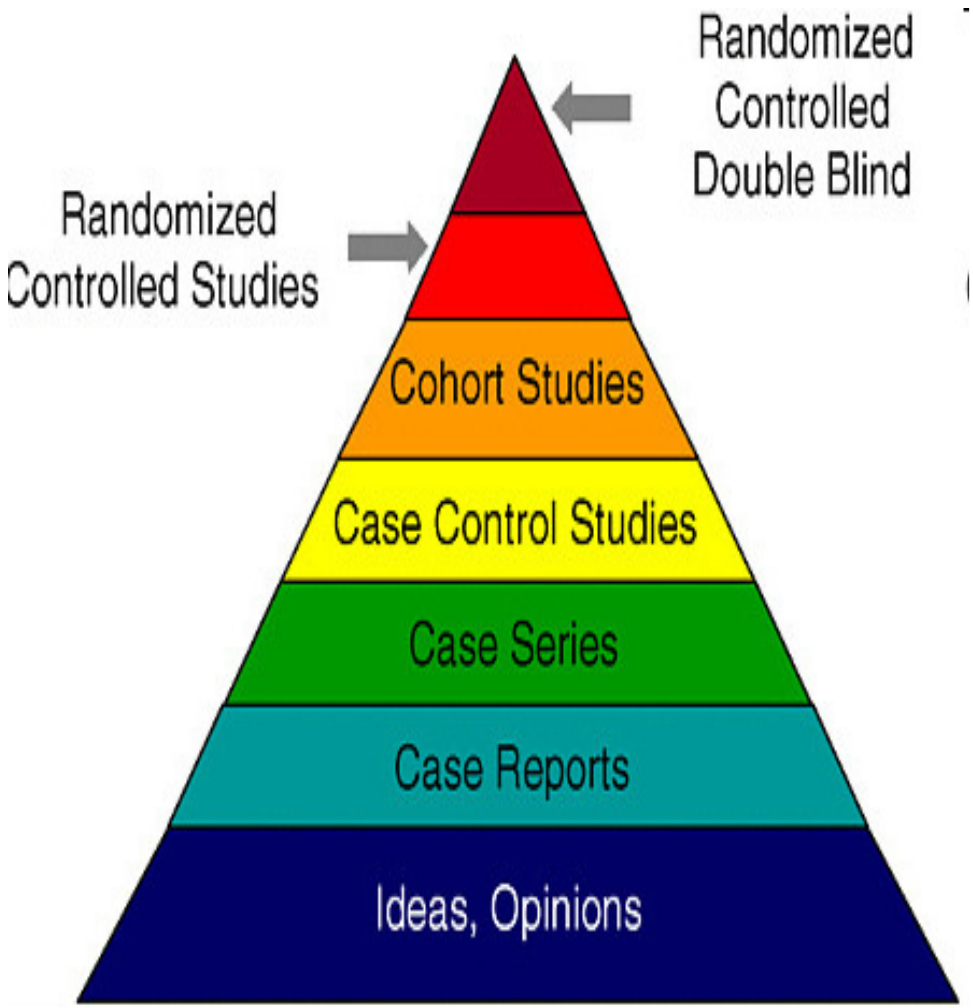
# Management and treatment of FOP patients

Meeting FOP Rome 24-26 March 2011

- **The strongest evidence for therapeutic interventions is provided by randomized, double-blind, placebo-controlled trials involving a homogeneous patient population and medical condition**



- **Patient testimonials, case reports, and even expert opinions have little value as proof because of the placebo effect, the biases inherent in observation and reporting of cases, and more**

# FOP therapy

- **As in other very rare diseases ,only anecdotal clinical experience using medications and expert opinions**
- **No clinical trials**
- **No specific treatment**

# THE MEDICAL MANAGEMENT OF FIBRODYSPLASIA OSSIFICANS PROGRESSIVA: CURRENT TREATMENT CONSIDERATIONS

The International Clinical Consortium
on
Fibrodysplasia Ossificans Progressiva
January 2011Guidelines

- **"We emphasize that this report reflects the authors' experience and opinions on the various classes of symptom-modifying medications, and is meant only as a guide to this controversial area of therapeutics. Although there are common physical features shared by every person who has FOP, there are differences among individuals that may alter the potential benefits or risks of any medication or class of medications discussed here. The decision to use or withhold a particular medication must ultimately rest with an individual patient and his or her physician".**

- **Class I:** Medications that have been widely used to control symptoms of the acute flare-up in FOP with anecdotal reports of favorable clinical results and generally minimal side effects
  - Short-term use of high-dose steroids
  - NSAIDs including the new anti-inflammatory and anti-angiogenic cox-2 inhibitors

- **Question** :Is treatment with NSAIDs recommended also in quiescent phases?

- **Answer** "That's a wonderful thought, but I do not know if the flare-ups are stopped despite the medications or if the medications help abrogate the ongoing flare-ups. It's difficult to know without a clinical trial. I'm reluctant to recommend stopping, although a brief holiday from the meds "now and then" may not be a bad idea as long as the clinical situation is well monitored. It's a tough call and probably needs to be individualized for each patient based on their sensitivity for recurrent flare-ups until we have better scientific evidence" Fred Kaplan

- **Class II: Medications that have theoretical application to FOP, are approved for the treatment of other disorders, and have limited and well-described effects. Can be added at the physicians' discretion**
  **-Leukotriene inhibitors**
  **-Mast cell stabilizers**
  **-Aminobisphosphonates**

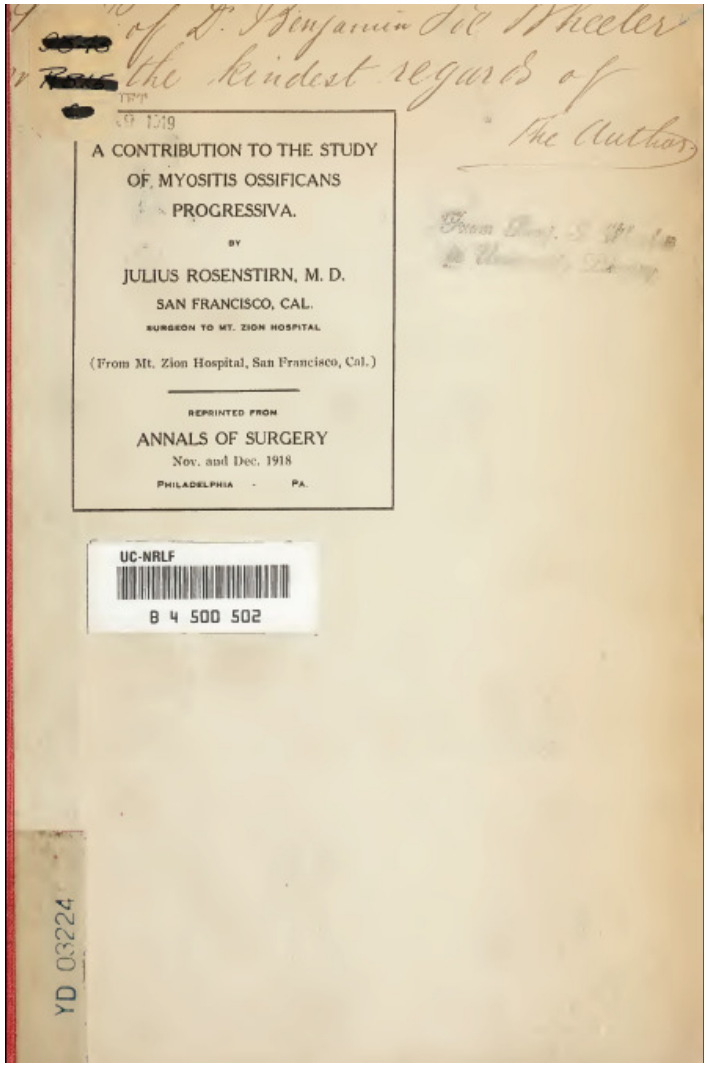
- **Class III: Medications under development and not yet available**
  **-ACVR1/ALK2 Signal Transduction Inhibitor**
  **-Monoclonal Antibody Against ACVR1/ALK2**
  **-Retinoic Acid Receptor Agonists**

# Other medications

- Calcium binders, mineralization inhibitors, antiangiogenic agents, fluoroquinolone antibiotics, retinoids, PPAR-gamma agonists, warfarin, rosiglitazone: only anectodal reports, no published series  available.
- One case reported in literature of successful surgical excision of heterotopic bone
- One case of successful surgical excision during treatment with i.m.diaminocillin (personal communication)

- **“Physicians treating patients who have FOP should keep in mind that none of these medications (or any other medications to date) have been proven to alter the natural history of FOP”**

**“The disease was attacked with all sorts of remedies and alternatives for faulty metabolism; every one of them with more or less marked success observed solely by its original author, but pronounced a complete failure by every other follower. In many cases, the symptoms of the disease disappear often spontaneously, so the therapeutic effect of any treatment should not be unreservedly endorsed.” (Rosenstirn, 1918).**



# FOP Therapy

Primum non nocere

First do no harm

# Management of FOP patients

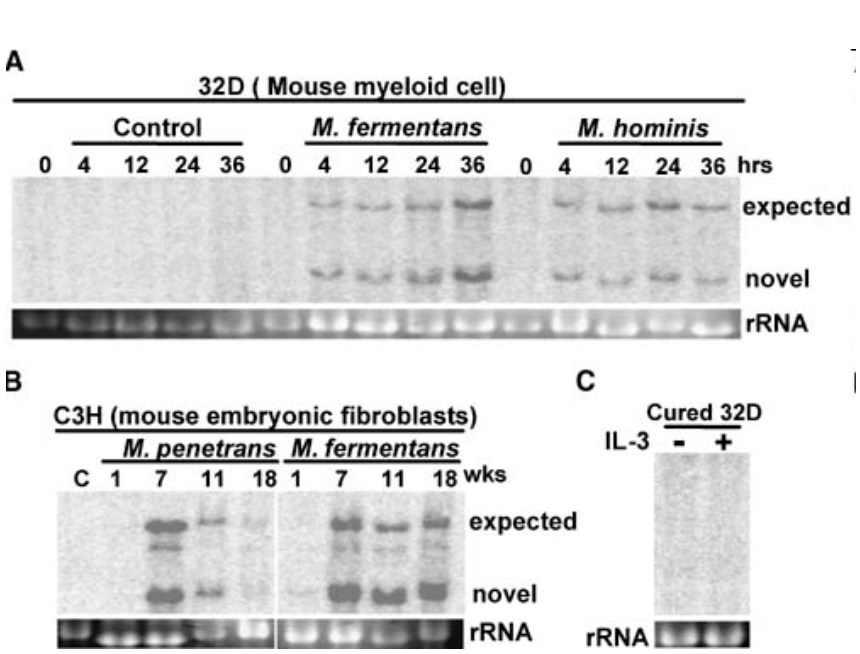
- Avoid soft tissue injuries, biopsies, surgical removal of heterotopic bone and all non-emergent surgical procedures
- Avoid passive range of motion
- Avoid intramuscular immunization
- Flu vaccine as an intradermal immunization
- Avoid intramuscular drug administration
- Avoid mandibular blocks, over-stretching of the jaw, and muscle fatigue.

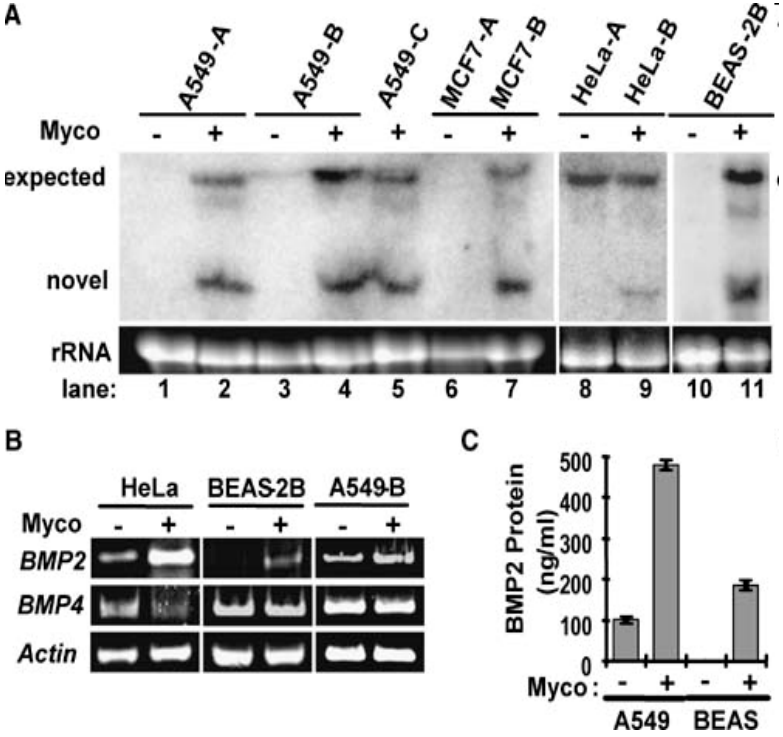
# Is flu the cause of flare-up?

Journal of Cellular Biochemistry 104:580–594 (2008)

## Mycoplasma Infection Transforms Normal Lung Cells and Induces Bone Morphogenetic Protein 2 Expression by Post-Transcriptional Mechanisms

Shan Jiang,[1] Shimin Zhang,[2] John Langenfeld,[3] Shyh-Ching Lo,[4] and Melissa B. Rogers[1]*



# Neurological complication

- Adult  complication?
- Neurodegeneration with brain iron accumulation?
- Link with ACVR1  mutation ?
- Treatment?

# FOP

- very rare genetic disease
- erratic natural history
- extreme interpersonal and intrapersonal variability
- no observational systematic study

# Do we need a multinational observational study ?

- **Aims:**
  **-improve understanding of clinical phenotypes of FOP and flare-up triggers**
  **-support the design and interpretation of future clinical trials with new drugs**
  **-inform and enhance the evaluation and care of patients with this disease**