

Management and Treatment of FOP- Patients



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Klinikum Garmisch-Partenkirchen




www.ifopa.org

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Welcome! The International FOP Association, or IFOPA, is a nonprofit support organization for families dealing with a rare genetic condition known as Fibrodysplasia Ossificans Progressiva (FOP). Simply stated, FOP causes muscles and other connective tissue to turn into bone, eventually causing immobility as FOP bone fuses joints.



The IFOPA's mission is to advance and support the Five Keys to a future without FOP. **RESEARCH**, the key to a treatment and cure. **EDUCATION**, the key to preventing misdiagnosis and finding more FOP families. **ADVOCACY**, the key to living independently with full equality. **HOPE**, the key to support, survival and community. **CURE**, the key to a better future for those with FOP & the people who love them.

The IFOPA's ultimate goal is to find a treatment and cure for FOP -- a true possibility now that the [FOP gene has been discovered](#). Until then, the work of the IFOPA continues, giving people with FOP hope that the future will bring earlier diagnosis, effective treatments and, one day, a cure.

News:

- **NEW VIDEO SERIES: FOP Facts & Insights** (YouTube)
- **NEW Penn Researchers Identify Source of Cells That Spur Aberrant Bone Growth**
- **NEW Classic and Atypical FOP Phenotypes Caused by Mutations in BMP Type I Receptor ACVR1** (PDF file - Adobe Acrobat required)
- **NEW Buy Educational Toys and Books, Raise Funds at MagicMountainToys.com**
- **NEW Tooth Ferrying** (article on FOP from TheScientist.com)
- **Unmasking the Mystery of FOP Fundraiser**
- **Important Editorial on FOP by Drs. Kaplan & Shore**
- **The Medical Management of FOP: Current Treatment Guidelines**
- **Penn Researchers Discover FOP Gene**
- **Download the IFOPA and FOP Facts in Brief sheets**

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The IFOPA's mission is to advance and support research, education, advocacy, and hope. Keys to a future with FOP are:

- RESEARCH**, the key to a better treatment and cure.
- EDUCATION**, the key to preventing misdiagnosis and finding more FOP families.
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**THE MEDICAL MANAGEMENT OF
FIBRODYSPLASIA OSSIFICANS PROGRESSIVA:
CURRENT TREATMENT CONSIDERATIONS**

The International Clinical Consortium
on
Fibrodysplasia Ossificans Progressiva¹

December 2008

From The Center for Research in FOP and Related Disorders,
The University of Pennsylvania School of Medicine, Philadelphia, PA 19104

Classes of Medications

Class I: Medications that have been widely used to control symptoms of the acute flare-up in FOP (swelling and pain), with anecdotal reports of favorable clinical results and generally minimal side effects. *Examples:* Short-term use of high-dose corticosteroids, and use of non-steroidal anti-inflammatory drugs (NSAIDs) including the new anti-inflammatory and anti-angiogenic cox-2 inhibitors.

Class II: Medications that have theoretical application to FOP, are approved for the treatment of other disorders, and have limited and well-described effects. *Examples:* Leukotriene inhibitors, mast cell stabilizers, and aminobisphosphonates (Pamidronate; Zoledronate).

Class III: Investigational new drugs
Examples: Signal transduction inhibitors and monoclonal antibodies targeting ACVR1 (presently under development).

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.

Dosing Informations

V. CLASSES OF MEDICATIONS (TABLE 1)					
CLASS I MEDICATIONS					
GENERIC	TRADE	CLASS	PROPOSED MECHANISM OF ACTION AS IT RELATES TO FOP	DOSING	MAJOR SIDE EFFECTS
Prednisone	Prednisone	Corticosteroid	Decreases lymphocyte and macrophage recruitment and tissue infiltration; potent anti-inflammatory drug; Decreases inflammation, swelling and edema especially when involving jaw, throat, and major joints. <i>Do not use for flare-ups involving chest or back (see text).</i>	2 mg/kg once daily by oral administration (PO) x 4 days maximum. Max dose: 150 mg/day. If flareup recurs immediately, may repeat 4 day course with longer taper. May also use longer treatment with taper for flare-ups in the submandibular region, especially those that affect breathing or swallowing. Should be started within 24 hours of the onset of a flare-up for maximal effectiveness. With the exception of life-threatening sub-mandibular flare-ups, do not use if the flare-up is more than two days old. (Medication should be taken with food). FOR PATIENTS IN INDIGENOUS REGIONS, ANTI-PARASITIC PRECAUTIONS MAY BE NECESSARY Alternatively, high dose intravenous corticosteroid (Prednisolone) therapy may be considered, but must be performed during an inpatient hospitalization to monitor for potentially dangerous side-effects of hypertension. The standard protocol for IV corticosteroid therapy is as follows: Day 1: 20-30 mg/kg of prednisolone IV Day 2: No medication Day 3: 20-30 mg/kg of Prednisolone IV Day 4: No medication Day 5: 20-30 mg/kg of Prednisolone IV. Total daily dose not to exceed 1000 mg.	~ avascular necrosis of hip ~ diabetes-cataracts ~ osteoporosis ~ chronic dependency ~ immune suppression ~ adrenal suppression ~ growth retardation ~ acne ~ peptic ulcers ~ hypertension ~ glaucoma ~ weight gain ~ skin bruising ~ sleep and mood disturbance
Ibuprofen	Advil Motrin	Non-steroidal anti-inflammatory medication (non-specific cox-1 and cox-2 inhibitor)	Anti-inflammatory and anti-angiogenic; symptomatic relief during a flare-up; Potential use in prevention by inhibiting inflammatory prostaglandins	Peds: 4-10 mg/kg PO every 6 hrs, as needed. Adult: 200-800 mg PO every 6 hrs, as needed. (Medication should be taken with food).	~ gastrointestinal bleeding ~ impaired renal function

Immunosuppression in FOP

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HEMATOPOIETIC STEM-CELL
CONTRIBUTION TO ECTOPIC SKELETOGENESIS

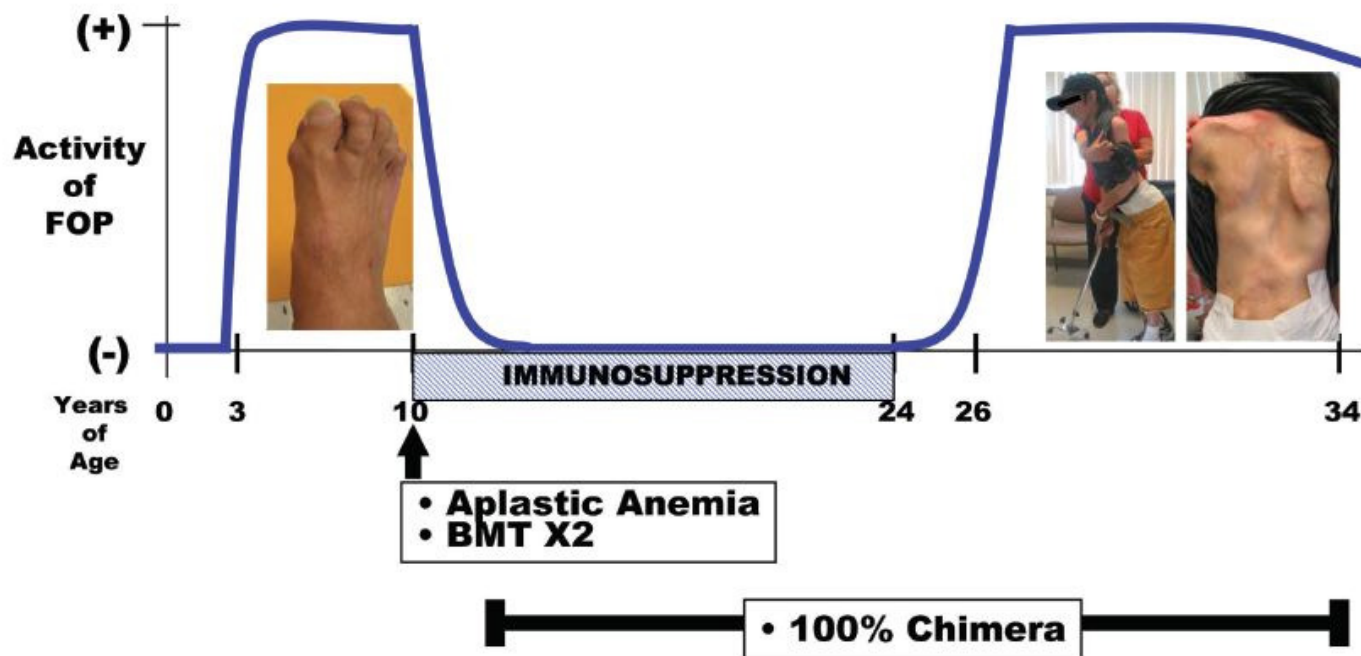


Fig. 1

Time line of the activity of the fibrodysplasia ossificans progressiva (FOP) in the patient before, during, and after bone marrow transplantation (BMT). The photographs, made when the patient was thirty-five years old, show the foot with a malformed great toe and him standing with assistance (side and back views). A photograph of the foot when the patient was a child was not available.

VI. SUMMARY OF KEY PRACTICE POINTS

This very brief guide will summarize the current symptomatic management of FOP (Kaplan et al., 2008).

Activities: Avoid soft tissue injuries, contact sports, overstretching of soft tissues, and muscle fatigue. Avoid biopsies, surgical removal of heterotopic bone and all non-emergent surgical procedures.

Anesthesia: If general anesthesia is required, perform awake intubation by nasotracheal fiber-optic technique. Highly-skilled FOP-aware anesthesiologists should be present for all elective intubations.

Falls: Locked upper limbs may accentuate head and neck trauma from falls. Epidural hematomas are common (surgical emergency). Use protective headgear in children who have upper limb involvement. All head and neck injuries must be evaluated immediately on an emergent basis.

Flare-up: (Back/chest): Use non-steroidal anti-inflammatory medications or cox-2 inhibitors with GI precautions. Use analgesics and/or muscle relaxants, as needed.

Flare-up: (Limbs/throat): Prednisone – 2 mgs/kg once daily (per oral) for four days; begin within first 24 hours of flare-up. Keep medication on-hand for emergencies. Use analgesics and/or muscle relaxants, as needed, with GI precautions.

Flare-ups (Protection): Most flare-ups result from over-use and soft tissue injuries. Prednisone - 2 mgs/kg, (per oral) once daily for three days to prevent flare-up after severe soft-tissue injury. Do not use after minor bumps or bruises.

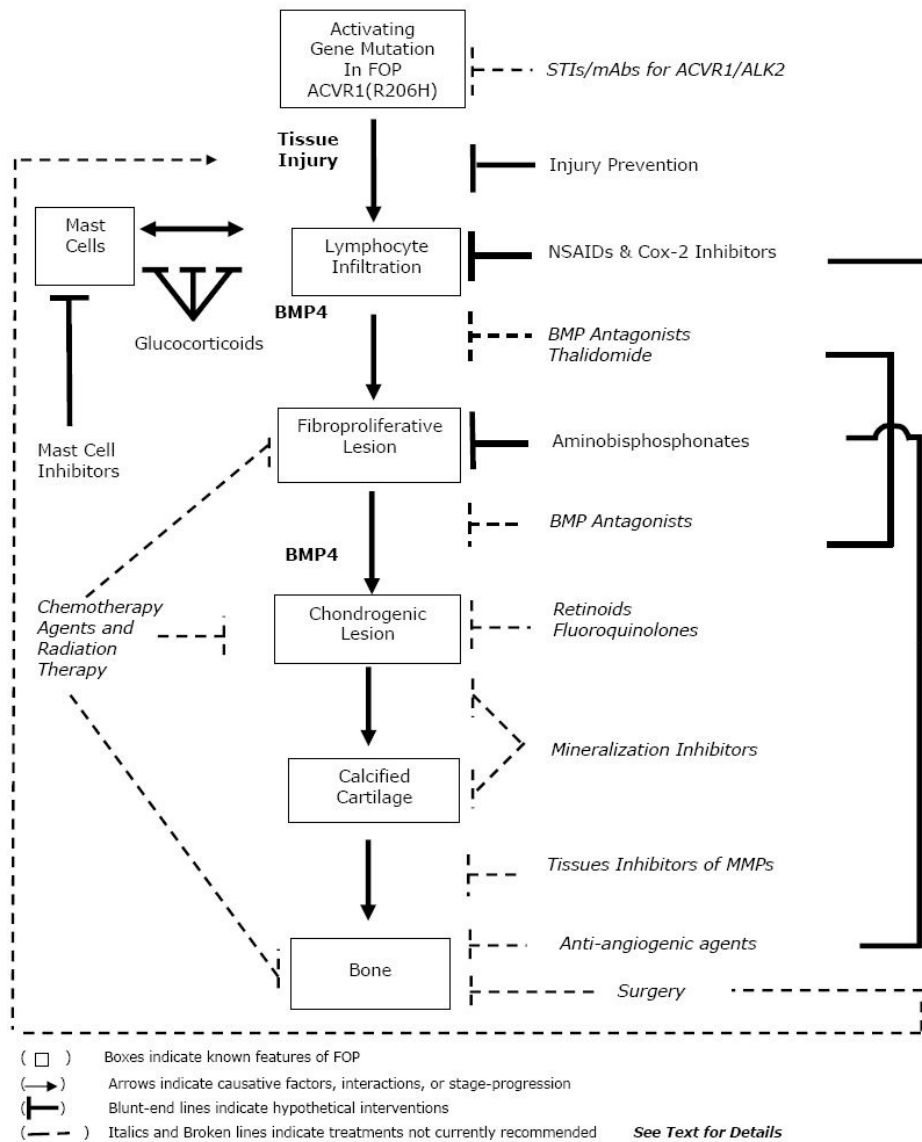
Hearing: Conductive hearing impairment is common. Perform periodic audiology evaluations. Hearing aids may improve conductive hearing loss.

Immunizations: Avoid all intramuscular immunizations. Subcutaneous immunizations are acceptable when FOP is quiescent. Avoid immunizations during flare-ups.

Influenza: Administer influenza vaccines subcutaneously, but never during flare-ups. Avoid live attenuated flu vaccine as it may cause flu-like symptoms and exacerbate FOP. Household contacts of FOP patients should be immunized annually. Cough suppression may alleviate stress on chest musculature.

Problem-
orientated
advice

FIGURE 1: SYMPTOMATIC TREATMENT SCHEMA IN FIBRODYSPLASIA OSSIFICANS PROGRESSIVA



Symptomatic
treatment
in FOP

Management: First visit (1)

- Check for typical anamnesis with heterotopic ossification
- Check for typical congenital malformations (Hallux valgus, malformed thumbs, osteochondromas etc.)
- XR: Hands, feet, neck, thorax, hips and knees
- Pulmonary function test and ECG

Management: First visit (2)

- Audiology evaluation
- Dental visit
- Genetic examination to verify the mutation
- Check the motor and joint function
- Therapy:
 - Consider continuous treatment with NSAID and montelukast
 - Corticosteroids for flare-ups
 - Trial of Pamidronate?

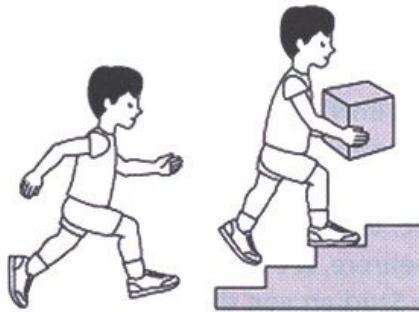
Further Management (3)

- Regular examinations by FOP-specialist every 6 months
- Regular examinations by pediatrician or family doctor every 2 months with lab tests when taking continuous drug therapy to monitor side-effects
- Dental visits once a year

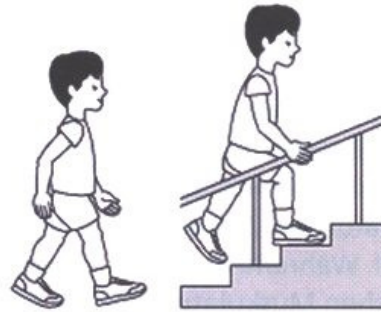
Further Management (4)

- Pulmonary function test and ECG once a year
- Audiology evaluations every other year till entering school
- Attendance of annual meetings as far as possible

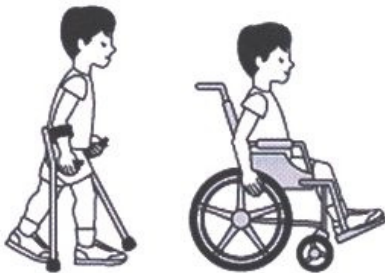
GMFCS



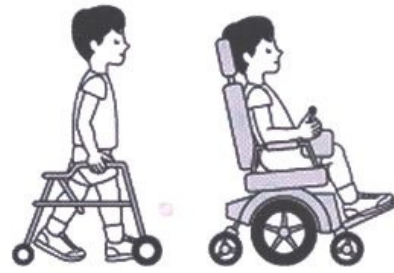
GMFCS Stufe 1



GMFCS Stufe 2



GMFCS Stufe 3



GMFCS Stufe 4



GMFCS Stufe 5

Gross Motor Function Classification System (GMFCS) for FOP- Patients

1 QUESTIONARIO PER LA VALUTAZIONE DELLO STATO DI SALUTE DEI BAMBINI (CHAQ)

2 Attraverso questo questionario ci proponiamo di ottenere informazioni su quanto la malattia limiti le attività quotidiane del suo bambino. Nel questionario scegliete, annerendo la casella corrispondente (☐ ☒ ☐), soltanto la risposta che meglio descrive le attività abituali del suo bambino **NELLA SETTIMANA PRECEDENTE A QUESTA VALUTAZIONE. ANNOTATE SOLO LE DIFFICOLTÀ O LE LIMITAZIONI DOVUTE ALLA MALATTIA.** Se il suo bambino ha difficoltà a svolgere determinate attività perché è troppo piccolo ma NON perché è LIMITATO DALLA MALATTIA, segnate "NON APPLICABILE". Sul retro di questa pagina potete aggiungere eventuali commenti.

3

	Senza alcuna difficoltà	Con qualche difficoltà	Con molta difficoltà	Incapace di farlo	Non applicabile
4 VESTIRSI E RIORDINARSI					
5 Il suo bambino è capace di:					
6 - vestirsi, allacciarsi le scarpe, abbottonarsi e sbottonarsi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7 - lavarsi i capelli	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8 - togliersi le calze	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9 - tagliarsi le unghie delle mani	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10 ALZARSI					
11 Il suo bambino è capace di:					
12 - alzarsi da una seggiolina o dal pavimento	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13 - mettersi a letto, alzarsi dal letto o alzarsi in piedi nel letto	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14 MANGIARE					
15 Il suo bambino è capace di:					
16 - tagliarsi la carne	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17 - portare una tazza o un bicchiere alla bocca	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
18 - aprire una scatola di biscotti nuova	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
19 CAMMINARE					
20 Il suo bambino è capace di:					
21 - camminare all'aperto su un terreno piano	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
22 - salire cinque gradini	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
23 *Indichi gli eventuali sussidi che il suo bambino usa abitualmente per le attività sopra elencate					
24 - bastone	<input type="checkbox"/>	- sussidi per vestirsi (bottoni a gancio, calzascarpe dal manico lungo, maglione con cerniere)			<input type="checkbox"/>
25 - girello	<input type="checkbox"/>	- matita fatta su misura o altri utensili speciali			<input type="checkbox"/>
26 - stampelle	<input type="checkbox"/>	- sedia speciale o costruita su misura			<input type="checkbox"/>
27 - sedia a rotelle	<input type="checkbox"/>	- altro (specifichi il tipo.....)			<input type="checkbox"/>
28 * Indichi ogni categoria per la quale il suo bambino abitualmente ha bisogno dell'aiuto di un'altra persona A CAUSA DELLA SUA MALATTIA					
29 - vestirsi e riordinarsi	<input type="checkbox"/>	- mangiare			<input type="checkbox"/>
30 - alzarsi	<input type="checkbox"/>	- camminare			<input type="checkbox"/>

Childhood Health Assessment Questionnaire



Thank you for your attention!