Periodic Paralysis Association: Annual Meeting

Challenges in the Diagnosis and Treatment of Hyperkalemic Periodic Paralysis

Robert C. Griggs, M.D.
Professor of Neurology, Professor of Medicine, Pathology and Laboratory Medicine, Pediatrics and
Center for Human Experimental Therapeutics
University of Rochester School of Medicine & Dentistry

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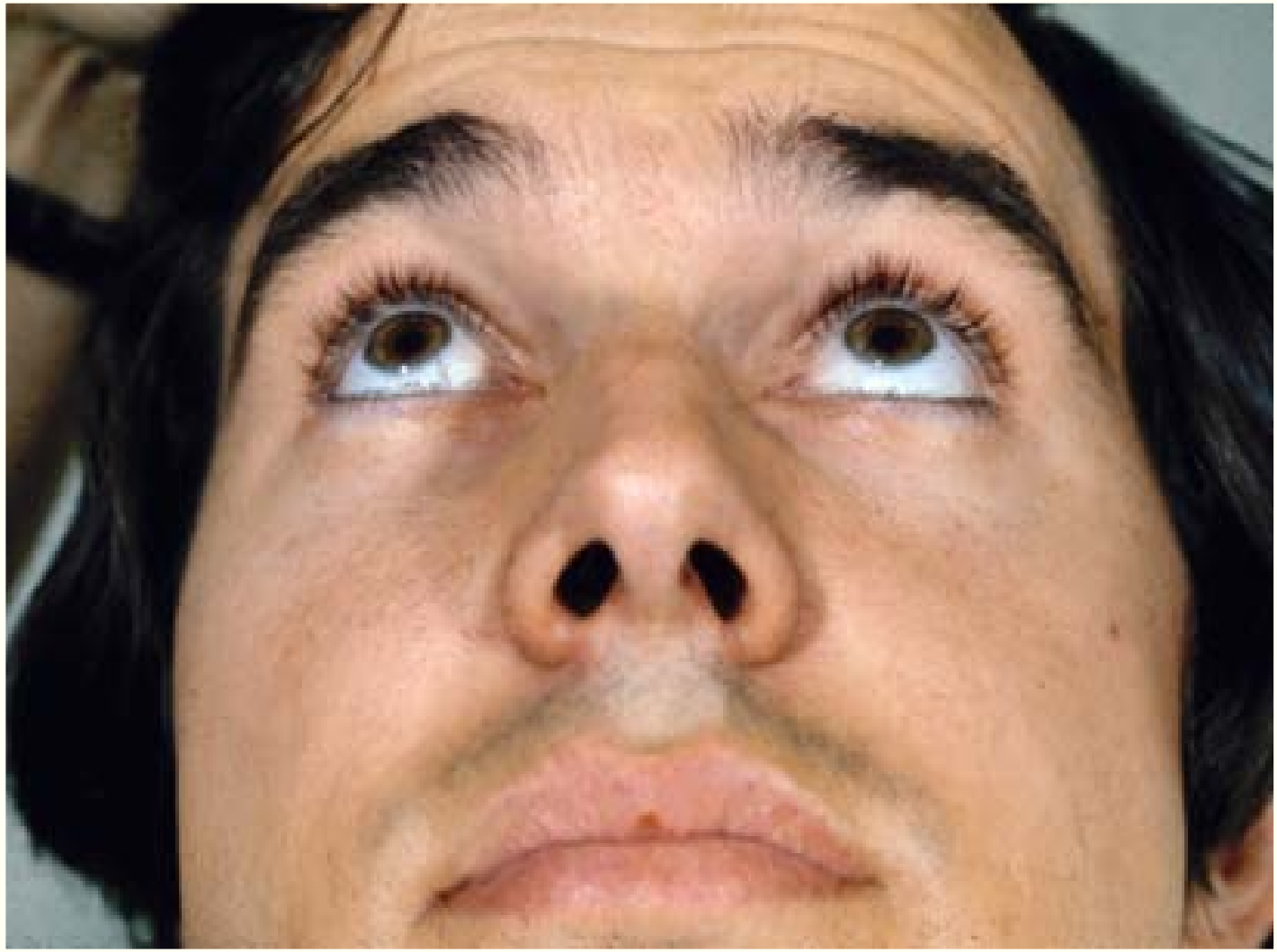
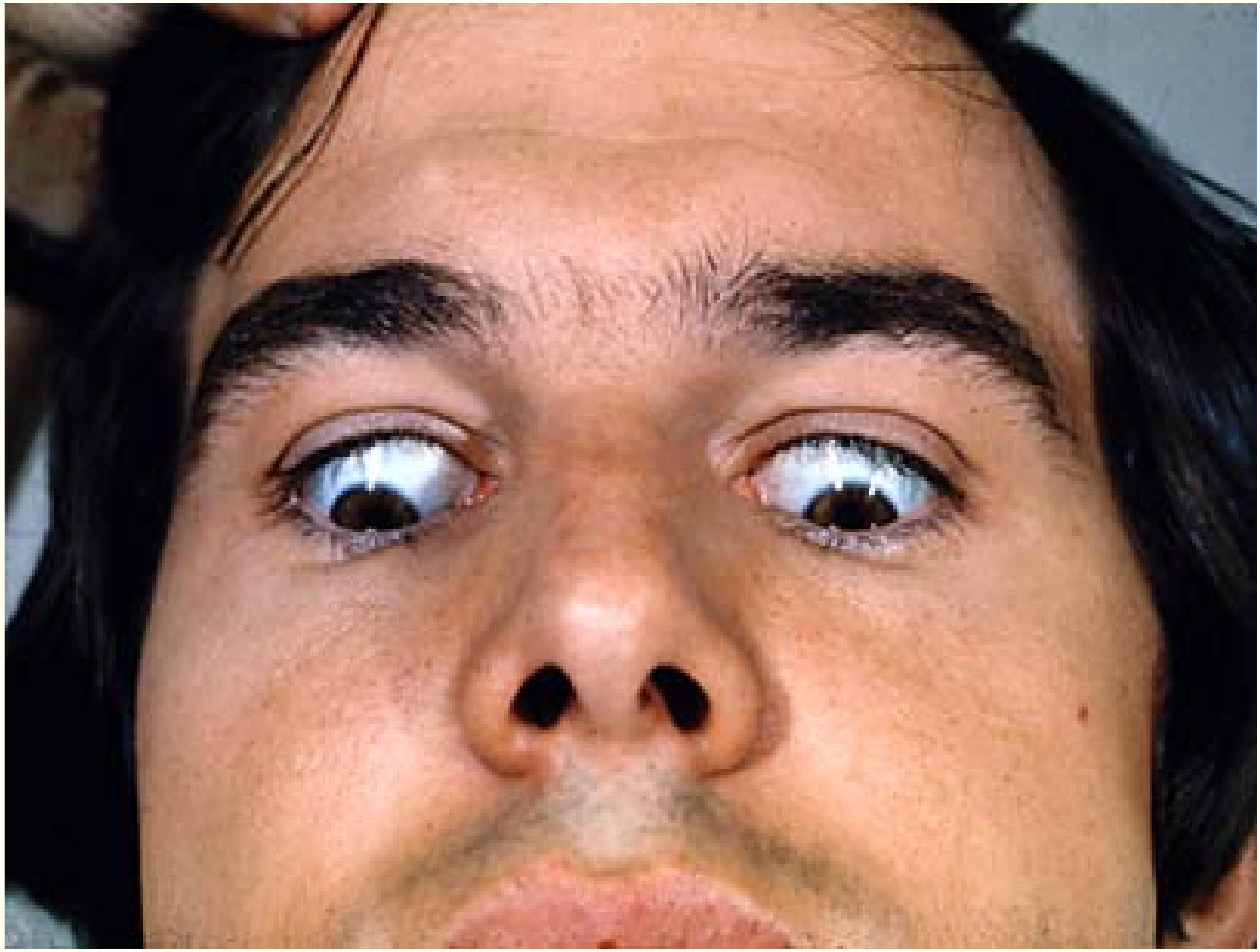
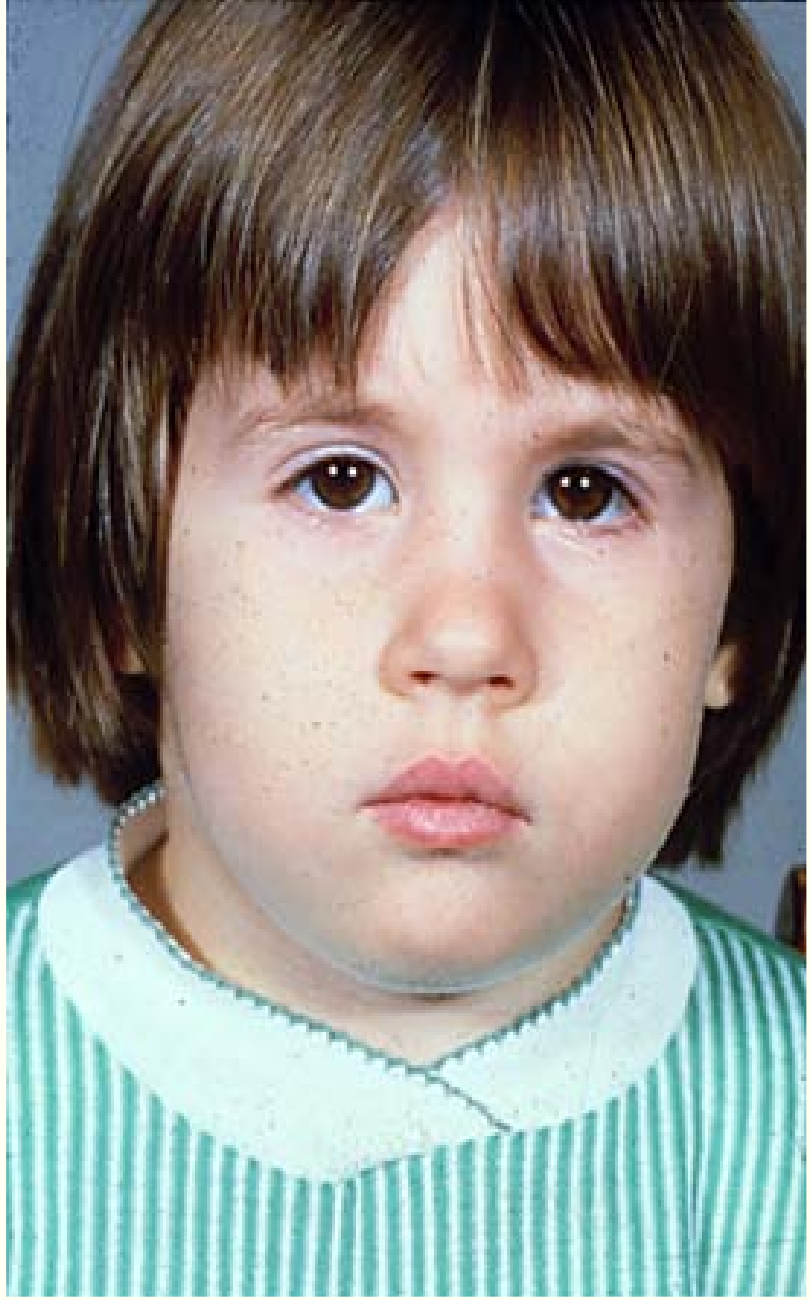
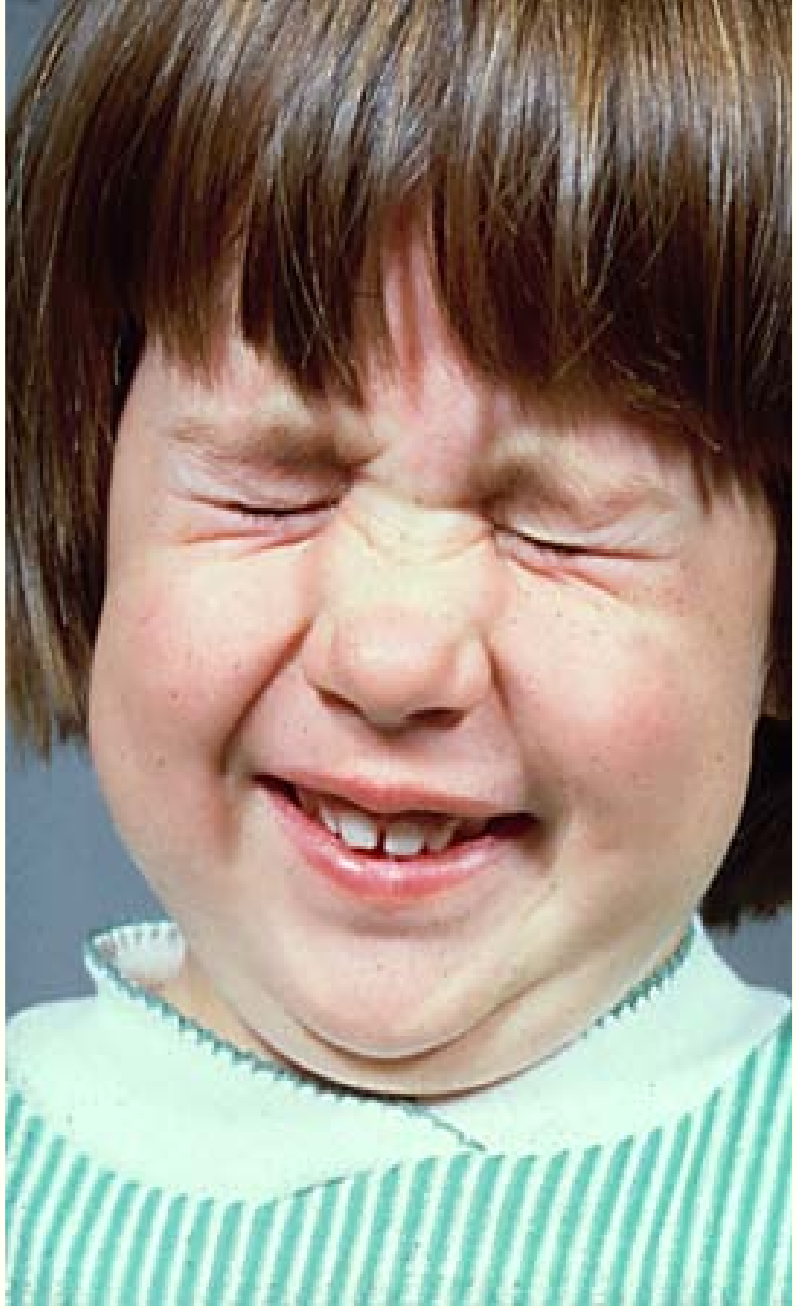
Hyperkalemic Periodic Paralysis – Clinical Features

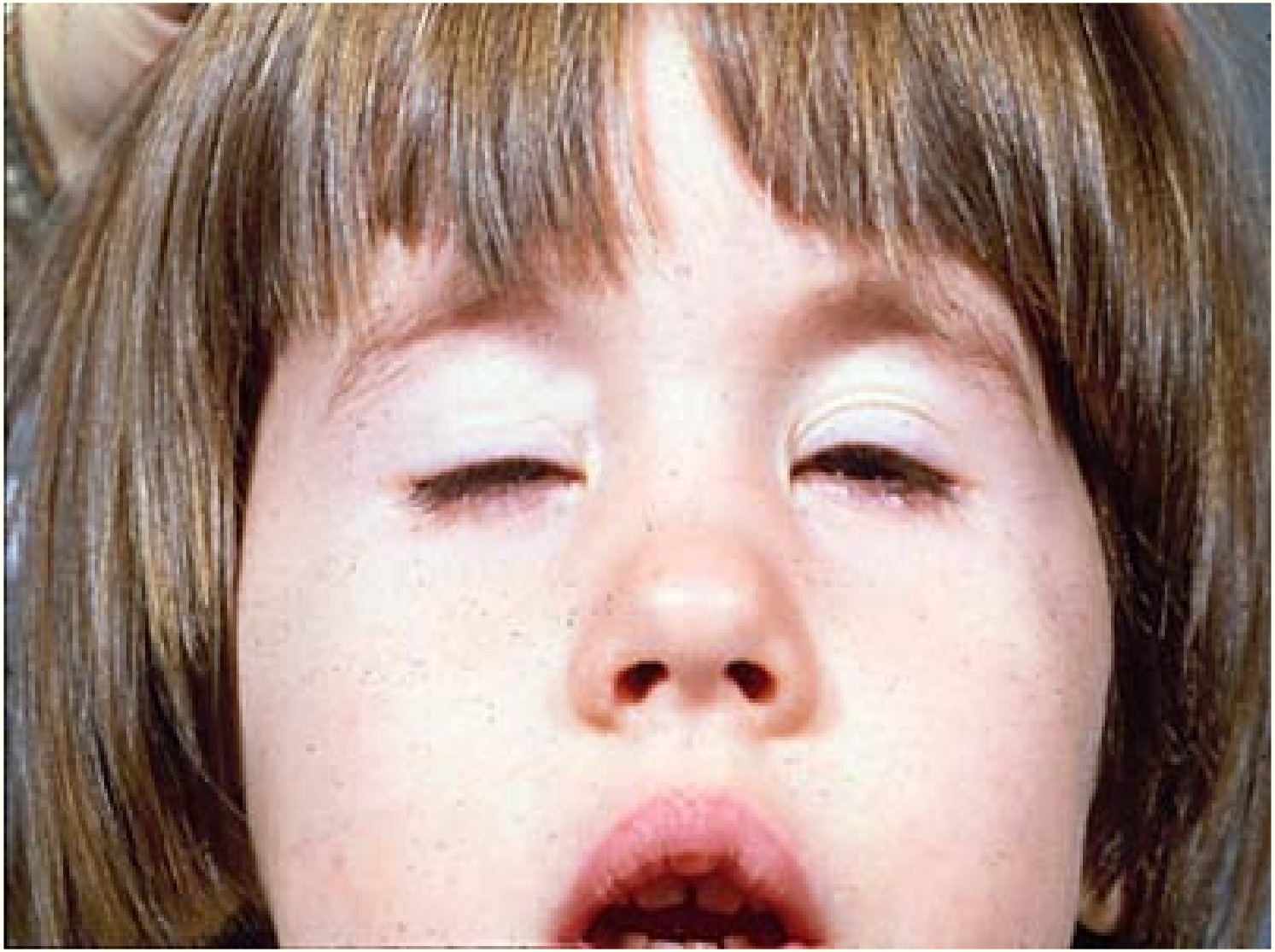
- Early onset – autosomal dominant
- With or without myotonia
- Overlap with paramyotonia congenita
- Brief attacks typical
- Interattack weakness: frequent and usually progressive











Diagnosis of Hyperkalemic Periodic Paralysis

- "Hyperkalemic" – a misnomer
- Wide fluctuations in serum K+
- Sodium (Na) channel mutations
- Provocative testing
  - Oral K-loading
  - Cold
- Exercise/EMG

Summary of Treatment: Acute attacks – Hyperkalemic Periodic Paralyses

- Rarely need acute treatment
- Oral glucose (not orange juice, etc.)
- β adrenegic inhaler
- Other strategies to treat hyperkalemia
  - IV glucose
  - Calcium infusion
  - Ion exchange resin

Preventive Treatment: Hyperkalemic Periodic Paralyses

- Remember potassium is not high in HyperKPP
- Carbonic anhydrase inhibitors
  - Acetazolamide
  - Dichlorphenamide (HYP HOP trial)
- Thiazides (may need K supplement)

Some Major Questions and Challenges in the Periodic Paralyses (1)

A. Prospects for returning dichlorphenamide to the market?

B. Treatment for patients who don't benefit from carbonic anhydrase inhibitors (acetazolamide, dichlorphenamide)?

C. If patients no longer have attacks of weakness, should they take treatment?

Some Major Questions and Challenges in the Periodic Paralyses (2)

D. What is the cause of weakness in mutation-negative periodic paralysis?

E. Is exercise good (or bad) for patients with periodic paralysis?

F. Should all patients with periodic paralysis --- even those without episodes of weakness --- be treated?

Other Information

- Update on HYP HOP clinical trial
- Update on Andersen-Tawil syndrome
- Some major questions in the field
- Summary of treatment

Prospects for Returning Dichlorphenamide to the Market?

- HYP-HOP study is continuing support by NINDS< MDA and Taro
- HYP HOP is the second major trail of dichlorphenamide in periodic paralysis
- Discussions with FDA
- Taro (now Sun Pharmaceuticals) has Orphan Product Designation

Treatment for Patients Who Don't Benefit from Carbonic Anhydrase Inhibitors (Acetazolamide, DCP)?

- Over 50% of patients

  (Matthews et al 2011)
- Aldosterone antagonists; triamterene
- Cautious K-supplementation

If Patients no Longer Have Attacks of Weakness, Should They Take Treatment?

- Motor signs before motor symptoms
- Sensory symptoms before sensory signs
- What is an "attack"?

What is the Cause of Weakness in Mutation-Negative Periodic Paralysis?

- Undetected mutation?
- A second gene (or genes)?
- What defines periodic paralysis?

Is Exercise Good (or Bad) for Patients with Periodic Paralysis?

- Attacks often occur with rest following exercise
- Exercise hastens recovery from weakness
- Weak muscles are susceptible to injury

Should all Patients with Periodic Paralysis --- Even Those Without Episodes of Weakness --- be Treated?

Hypotheses:

- All patients with periodic paralysis are weak at all times
- Patients are often unaware of episodes of weakness
- Recurrent attacks injure muscles

Update on the HYP HOP Trial (1)

- Goals of study
  - Confirm that dichlorphenamide prevents attacks of weakness in hypokalemic periodic paralyses and hyperkalemic periodic paralysis
  - Establishes that dichlorphenamide is safe for long-term use
  - Determine if dichlorphenamide improves strength

Update on the HYP HOP Trial (2)

Centers recruiting:

- University of Rochester, Emma Ciafaloni, MD
- Columbia University Medical Center, Hiroshi Mitsumoto, MD
- Ohio State University, John Kissel, MD
- Washington University School of Medicine, Alan Pestronk, MD
- University of Kansas Medical Center, Richard Barohn, MD
- UCLA, Perry Shieh, MD
- Brigham & Women's Hospital, Anthony Amato, MD
- University of California San Francisco, Jeffrey Ralph, MD, Louis Ptacek, MD
- University of Texas Southwestern, Jaya Trivedi, MD, Steve Cannon, MD
- Mayo Clinic, Brian Crum, MD
- Hopital Pitie-Salpetriere, Bertrand Fontaine, MD, PhD, Savine Vicart, MD
- University of Milan, Giovanni Meola, MD, Valeria Sansone, MD
- Institute of Neurology, Michael Hanna, MD

Summary of Treatment: Acute attacks – Hypokalemic Periodic Paralyses

- Oral potassium supplementation
- If unable to swallow or if vomiting: IV potassium bolus – 4-6 mEq
- Why mannitol?

Preventive Treatment: Hypokalemic Periodic Paralyses

- Avoid provocative factors (carb, stress, exercise)
- Potassium supplements: surprisingly little benefit
- Carbonic anhydrase inhibitors ± potassium
- Potassium-sparing diuretics ± potassium preparations (caution)
- New Agents?

Andersen-Tawil Syndrome: Current Issues

- Discovering the cause(s) of ATS-2 (ATS-3, etc.)
- Defining the best treatment for:
  - Episodes of weakness
  - Fixed interattack weakness
  - Cardiac arrhythmias
  - Behavioral disorders
  - Cosmetic aspects

Acknowledgements

- CINCH Investigators
- Muscle Study Group
- The HYP HOP team
- Our patients and the Periodic Paralysis Association