Adolescent Therapeutics Working Group Presentation

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Adolescence (noun, 15th century)

Pronunciation: \a-də-ˈle-sən(t)s\

1. the state or process of growing up

2. the period of life from puberty to maturity terminating legally at the age of majority

3. a stage of development (as of a language or culture) prior to maturity
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- Population
- Care providers
- Conditions
  - Puberty
  - Disease
Adolescent Therapeutics Population

- **Individuals between 10-24 years represent**
  - 26.8% of total world population
  - 19.0% of the more developed (western) world
  - 28.5% of the less developed world

- **Individuals between 40-64 years represent**
  - 24.5% of total world population
  - 33.2% of the more developed (western) world
  - 22.5% of the less developed world
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Care Providers

Concerns all specialists:
- Pediatrics
- Internal Medicine
- Family Medicine
- Gynecology
- Surgery
- Pharmacology

Focus upon issues that affect adolescents

Adolescent therapeutics can be defined by:
- Age (Typically 12-24 years of age)
- Behavior (Risk and Prevention)
- Specific Diseases and Developmental Stages
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Puberty

- Changes hormonal influence
- Changes body composition
- Changes in disease processes
- Changes in metabolism
- Changes in adherence
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Conditions

- Prevention
  - Primary
  - Secondary

- Treatment
  - Acute conditions
  - Chronic conditions

- Compliance

- Development
  - Normal
  - Abnormal
  - Disease

- Growth
  - Height
  - Weight
  - Pubertal status
  - Hormonal status
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Conditions (partial list)

- Acne
- Asthma
- Diabetes Mellitus
- Infectious Diseases
- Injuries
- Hypercholesterolemia
- Hypertension
- Menstrual Disorders
- Migraines
- Osteoporosis
- Pregnancy
- Obesity
- Depression
- Anxiety
- OCD
- Bipolar Disorder
- ADHD
- Substance Abuse
Ever increasing issue

Changes in BMI (no change in Lean BMI)

Changes in disease manifestation

Changes in PK/PD
Common chronic disease in children

176,500 people under the age of 20 (1:400-600 children with Type 1)

Nearly 75% of newly diagnosed Type 1 diabetes < 18 years old

Adolescents with newly diagnosed type 2 diabetes increased from < 5 % to 30 – 50%
Understand the effects of both pubertal development and body weight on pharmacokinetics, pharmacodynamics, pharmacogenetics of pharmaceutical agents in children and adolescents.
With particular emphasis on understanding:

- The effect of both stage of sexual maturity and body weight on drug distribution and metabolism
- Pharmacogenetic changes in the expression of drug metabolizing enzymes in adolescents related to age, family history and pubertal maturation
- Extent and mechanism, risk factors and consequences of weight gain seen in older children and adolescents treated with antipsychotics, parenteral contraceptives and other agents associated with weight gain
- Impact of adherence on the pharmacotherapy and therapeutic outcome in adolescents since adolescents frequently are responsible for managing their own medications and treatments
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Study Design

- Systematic improvements
- Expertise development
- Comprehensive approach
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Study Design Considerations

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- Assent vs. Consent
- Regulatory Issues
- Pregnancy risk is always an issue
- Study design needs to take into account
  - Dosage scaling
  - Developmental considerations
  - Pubertal staging
  - Intrusiveness/inconvenience
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Study Design Considerations

- Highly motivated study population
- Recruitment of additional participants
- Technically savvy
  - e-diaries
  - text messages
  - cell phones
- If they have a chronic disease – typically only one (decreased comorbid conditions)
- Honest (sometimes brutally honest)
- Adherence rates similar to adults
Develop a protocol across review divisions within FDA to evaluate the endocrine and metabolic, psychological, and reproductive impact of pharmacotherapy in adolescents (with particular emphasis on psychotropic and other drugs frequently used in adolescents)
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Dosing Information

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- Fit the individual
- Logically designed
- Carefully determined
- Eliminate errors
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Priority 3

- Develop understanding of how and where to distinguish between pediatric (preadolescent) and adult dosing guidelines for all drugs used in adolescence.
Determine when weight and/or age based dosing regimens are no longer applicable (e.g. When administering HIV drugs for a 12 year old who is at/or above adult weight or in a young adult who is significantly below adult weight).

Determine whether development of the specific adolescent dosing guidelines needs to be considered for the therapeutic agents most commonly used within adolescents and young adults.
The Adolescent Therapeutics Working Group felt that adherence and adherence readiness of the adolescent as a key component of effectiveness for those drugs that demonstrate efficacy in the general adult populations.
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Committee Members

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Center for Drug Evaluation and Research
U.S. Food And Drug Administration

- Rosemary Addy, MHS
- Felicia Collins, MD, MPH, FAAP
- Beth Durmowicz, MD
- Oluchi Elekwachi, PharmD, MPH
- Alyson Karesh, MD
- Lisa Mathis, MD, CDR, USPHS
- Paul Reed, MD
- Hari Cheryl Sachs, MD
- Amy Taylor, MD, MHS, FAAP
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Office of the Commissioner
U.S. Food and Drug Administration

- Debbie Avant, RPh
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- Anna Myers, RPh, MPH
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Committee Members

National Institutes of Health

- Jonathan Goldsmith, MD
  National Heart, Lung and Blood Institute
- Richard L. Gorman, MD
  National Institute of Allergy and Infectious Diseases
- Roberta Kahn, MD
  National Institute on Drug Abuse
Adolescent Therapeutics Committee Members

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- Bill G. Kapogiannis, MD
- Jan Leahey
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- Tina K. Urv, PhD
- Anne Zajicek, MD
- Eunice Kennedy Shriver

National Institute of Child Health and Human Development
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Institutional and Business Community

- Jeffrey Blumer, MD, PhD
  Case Western Reserve University
  Rainbow Babies and Childrens Hospital

- Bernard Brownstein, MD
  Premier Research Group

- Randall Clark, MD
  The Children's Hospital, Denver

- Lawrence D'Angelo, MD, MPH
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- S. Jean Emans, MD
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  Impaq International

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  University of Wisconsin School of Medicine and Public Health

- **Pamela Murray, MD, MPH**
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- **Natella Rakhmanina, MD, FAAP, AAHIVS**
  Children's National Medical Center
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- **Maria Trent, MD, MPH**
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- **Kathy Woodward, MD**
  Children's National Medical Center
Thank you for your time and attention