

THE MATURING WOMAN WITH RETT SYNDROME

From Puberty to Menopause

Together We Are Better

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**Jane Lane, RN, BSN
University of Alabama at Birmingham**

Points for Discussion

- **Puberty, Menarche, and Menopause**
- **Seizure and Antiepileptic Medication Issues in Women**
- **Medications and Procedures for Menstrual Management**
- **Health Maintenance**
- **Behavior and Social Issues**
- **Longevity**

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Puberty 101

“Adolescence is a period of rapid changes.

Between the ages of 12 and 17, for example, a parent ages as much as 20 years.”

- Anonymous

Onset of Puberty in Rett Syndrome

No different from other females

- Age of onset of puberty variable
 - Usual onset 8 – 13 years
 - Occurring younger than in past generations, but may also begin in teens
- Factors that affect onset of age
 - Nutrition
 - *Synthetic hormones in food* theory
 - Activity level
 - Genetics
 - Antiepileptic medications
 - Abnormal hormone level – precocious puberty

Hormones and Puberty

- **Hormones start the process that effect major, lasting changes**
- **Body changes**
 - Growth spurt
 - Breast development
 - Hips wide
 - Pubic, underarm and leg hair thickens and darkens
 - Oily skin and hair
- **May experience cramps, mood swings, irritability and fatigue**
- **Eventually will enter menarche**
 - 2 years after puberty; entire process usually takes 4 years

Hormone Production

- Hypothalamus (in the brain) starts to release pulses of hormones every 90 minutes or so.
- This stimulates the pituitary gland (also in the brain) to produce *luteinizing hormone (LH)* and *follicle stimulating hormone (FSH)*.
- LH and FSH have roles with egg maturation and release and cause ovaries to start producing other hormones – called *sex hormones*.

Sex Hormones

■ Estrogen

- Stimulates breast development
- Causes vagina, uterus and Fallopian tubes to mature
- Plays roll in growth spurt and alters distribution on fat onto hips, buttocks, and thighs

■ Progesterone

■ Testosterone (in very small amounts in girls)

- Promotes muscle and bone growth

The Effects of Hormones on Cycles

- **One egg (out of several hundred thousands) in the ovary becomes mature and is released from the ovary to begin the journey down the Fallopian tube and into the uterus**
- **If egg is not fertilized, the levels of estrogen and progesterone begin to fall**
- **Without the supporting action of the hormones, the lining of the uterus is shed - “menses”**

Menarche

- **Marked by start of menstrual cycle**
- **Age of onset in RS mirrors general female population ~2-4 years after puberty onset**
- **African-American females can achieve menarche at an earlier age than Caucasian females**
- **May come in “like a lion or lamb”**
- **May be irregular**

Related Issues To Menstruation

- **Cramps**
 - Meds OTC or Prescription
 - Warm packs, baths and massage
 - Exercise
- **PMS**
 - Tender breasts, bloating, irritability, low mood
 - Possible causes: Hormone fluctuations, changes in brain chemicals
- **Hygiene**
 - Menstrual flow is odorless until it comes in contact with air and bacteria
 - Bathing and meticulous personal care essential
- **Seizures**

**Puberty and Menstruation are
NORMAL functions**

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**Seizures, Puberty, Menstruation
and
Antiepileptic Medications**

Relationship Between Seizures and Hormones

- **Hormones do not cause seizures, but influence the occurrence**
 - **Estrogen – excitatory affect on brain cells**
 - **Progesterone – inhibitory affect on brain cells**

Relationship Between Seizures and Hormones

- Seizures that worsen or occur only during ovulation or just prior to or during menstruation are called *Catamenial epilepsy* and are caused by estrogen and progesterone fluctuations

Seizures and Puberty

- Seizures may increase during puberty
 - Hormone fluctuations
 - Antiepileptic medication doses may not be adequate due to rapid weight increases
- Check medication blood levels

AEDs and Puberty

- 1988 study by Galli, et al looked at 57 epileptic subjects from 6-15 years on AED for at least 2 years
 - Onset of stage II puberty occurred significantly earlier in males and females than healthy controls

Seizures and Menstruation

- **Seizures may increase during menstruation**
 - Hormone fluctuations
 - Fluid retention
 - Reduced blood levels of medications
 - Sleep disruption
- **Menstrual cycles may be changed by seizures**
 - 30-50% of women with temporal lobe epilepsy compared to 7% of women without epilepsy

Catamenial Epilepsy Treatment Options

- **Intermittent perimenstrual medications**
 - clonazepam (0.05-0.1mg/kg/day) or clobazam (5-10mg/day; up to 30mg/day)
- **Hormonal manipulation aimed at increasing progesterone**
 - Progesterone (days 10-26 of cycle)
 - Combination oral contraceptive
- **Diuretics**
 - Diamox
- **Sleep medications**

Effects of Antiepileptics on Oral Contraceptives

- **Some increase the breakdown of contraceptives, making them less effective**
 - Tegretol, Carbatrol, Trileptal, Dilantin, Phenobarb, Mysoline, Topamax
- **Some do not increase the breakdown of contraceptives; may increase hormone levels**
 - Depakote and Felbatol
- **Some have no effect on contraceptives**
 - Neurontin, Lamictal, Keppra, and Gabitril

Effects of Oral Contraceptives on Antiepileptics

■ *Lamictal*

- OC increases clearance, so more AED may be required to have good seizure control.
- At end of placebo week, trough AED level may be 2X what it was at end of active drug weeks.
- Good argument for around the calendar oral contraceptives (i.e. Seasonale, Seasonique, Lybrel)

Effects of Oral Contraceptives on Antiepileptics

■ *Dilantin*

- Serum drug levels increased by estrogen
- May require AED level assessment after estrogen therapy begun

Effects of Oral Contraceptives on Antiepileptics

- ***Depakote and Tegretol***
 - No known effects from oral contraceptives

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**Medications and
Procedures for Menstrual
Management and Birth
Control**

Menstruation Management

- Non-interventional method or the “we’ll *just deal with it*” approach
- Oral Contraceptives (“BCP’s”)
- Depo-Provera injection
- Endometrial Ablation
- Hysterectomy

Oral Contraceptives

- **Conventional – 21 or 28 day course, menstruation every month**
 - Yasmin[®], LoEstrin[®], Ortho Tricyclen[®], and Ortho Tricyclen Lo[®] (low estrogen)
- **Newer – 84 day course, reduces menstruation 4X/year**
 - Seasonale[®], Seasonique[®]
- **Newest – taken daily and continuously, stops menstruation**
 - Lybrel[®]

Risks of Oral Contraceptives

- **Common: dizziness, headache, nausea, mood changes, weight gain, breakthrough bleeding**
- **Rare: blood clots, high blood pressure, stroke, heart attack**

Depo-Provera Injections

- Progesterone
- Must be given by RN or MD
- Should prevent ovulation, but 30% continue to have regular cycle
- Administered every 3 months
- Affects bone density increasing risk of osteoporosis
- Side effects may be extreme and irreversible until medication wears off
- Include irritability, weight gain, irregular break-through bleeding

Endometrial Ablation

- **Outpatient surgery**
 - Laser, heat, electricity or freezing
 - Local, spinal or general anesthesia
- **Mechanism of action**
 - Endometrium scars reducing flow
- **Permanently stops menstruation in about 50%, reduces flow in most of remaining 50%**
 - More effective in older than younger
 - Adjunctive use of gonadotropin-releasing hormone (Lupron) may improve effectiveness
- **Risks – laceration, burns, usual surgery risks**
- **Short recovery**

Hysterectomy

- **Surgical removal of uterus +/- ovaries**
 - Total – uterus and cervix
 - Subtotal – uterus only
- **Techniques**
 - Abdominal
 - Mini Laparotomy
 - Vaginal
 - Laparoscopy
- **Risks and Disadvantages**
 - Usual surgery risks
 - Long recovery

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Menopause 101

**“Grow old along with me! The
best is yet to be”....**

-Robert Browning

Menopause in RS

- **Average age on onset - 51 years (40-65)**
- **Anecdotal reports with RS suggest early aging in appearance, but unsure of impact on age of menopause**
- **Changes that occur**
 - **Ovaries stop making estrogen**
 - **Change in periods 1st sign - until they stop**

Menopause and Seizures

- Generally occurs significantly earlier in women with high seizure frequency
- Reports of seizures during menopause
 - 40% report worsening seizures
 - 27% report improvement of seizures
 - 33% report no change
- Hormone replacement therapy associated with increase in seizures (more in those with catamenial epilepsy)
- In RS, seizures diminish and EEG's tend to improve as women grow older

Menopause Health Issues

- Osteoporosis – long term AED increase risk
- Mood changes
- Hot flashes
- Increased chance of bladder infections
- Abnormal bleeding may occur
- Hormone replacement therapy may be given to offset symptoms such as hot flashes, bone loss, mood disturbances, but come with their own risks (increased seizures and cancers of breast and endometrium)

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Health Maintenance

Health Maintenance Fact

- **Women with disabilities receive less breast and cervical health care as a result of environmental, attitudinal, and information barriers**
 - **Inaccessible health care facilities**
 - **Lack of disability awareness by clinicians**
 - **Dependence on others for self-exams**
 - **May be unable to report symptoms**

Health Maintenance Fact #2

- **Women with disabilities tend to be diagnosed with breast cancer at later stages and have higher mortality rates**

Roetzheim, et al , J. of Health Care for the Poor and Underserved, 2002

Health Maintenance

- No assumption about a woman's health care needs should be based on the nature and extent of her disability
- Regular screening necessary to ensure good health and prevent common disease

Health Maintenance Schedules

■ Breast Health

- Monthly home exam from age 18 years
- Yearly professional exam

■ Pelvic exams and PAP smears

- Yearly at age 18 years or when birth control begun

■ Other screenings of aging

- Yearly professional exam with age appropriate screenings

■ Bone density

- DEXA scan if bone health in question or if on AED

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Nutrition

Nutrition in Adolescence

- Nutritional needs greater than any other time after the newborn period
- Increased need for calories, proteins, vitamins and minerals
- Normally might expect ~50 to 60 pound weight gain from age 9 to 17
- Normal in RS – who knows?

Nutrition in Adults

- Decreased need for calories
- Increased need for Calcium (after menopause)
- Increased need for fiber
- BMI (Body Mass Index)
 - Good indicator of nutritional health
- Normal in RS – who knows?

Body Mass Index

- **Calculation:** $\text{Weight (lbs)} \div \text{Height (in)} \div \text{Height (in)} \times 703 = \text{kilograms per meter squared (kg/m}^2\text{)}$
- **BMI categories:**
 - Underweight $\leq 18.5 \text{ kg/m}^2$
 - Normal weight = $18.5 - 24.9 \text{ kg/m}^2$
 - Overweight = $25 - 29.9 \text{ kg/m}^2$
 - Obese = BMI of 30 kg/m^2 or greater

Average Daily Nutritional Needs in Adolescent Females

- **Calories - 2000 kcals**
- **Protein - 46 grams**
- **Calcium - 800 to 1300 mg**
- **Iron - 8mg**
- **Zinc - 7 mg**
- **Folate - 330 ug**
- **Vitamin A - 485 ug**
- **Vitamin B₆ - 1 ug**
- **Adequate fluids - 6 to 8 cups fluid per day-more in hot weather**
- **Adequate fiber - Age plus 5 grams-more?**

2004 Food and Nutrition Board – National Academy of Sciences

Average Daily Nutritional Needs in Adult* Females

- **Calories - ~1500 kcal – varies with activity**
- **Protein - 46 grams**
- **Calcium - 1000 milligrams (1200 mg after menopause)**
- **Iron - 5-8 milligrams (depending on age)**
- **Zinc - 7 milligrams**
- **Folate - 330 micrograms**
- **Vitamin A - 485 micrograms**
- **Vitamin B₆ – 1 micrograms**
- **Adequate fluids - 6 to 8 cups fluid per day-more in hot weather**
- **Adequate fiber- 25 grams**

2004 Food and Nutrition Board – National Academy of Sciences

***Adult = 24 months after menarche**

Nutritional Bottom Line

- Does your daughter look healthy?
- Does your daughter seem happy and content?

Nutrition Websites

- American Dietetic Association
<http://www.eatright.org>
- Nutrient Recommendations-DRI's
<http://www.nap.edu>
- Food Guide Pyramid 2005
<http://www.mypyramid.gov>
- Pediatric Health and Nutrition
<http://www.brightfutures.org>

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**Behavioral and Social
Issues**

Changes in Behavior

Irritability

- **Physiological Causes**

- Many

- **Non-physiological Causes**

- Frustration

- Boredom

Physiological Causes of Irritability

- **Gastro-esophageal reflux (“heartburn”)**
- **Cholecystitis (gallbladder disease)**
- **Constipation**
- **UTI**
- **Orthopedic Issues**
- **Dental Problems**
- **Sleep Deprivation**
- **Common Aches and Pains**
- **Hormonal Changes**

Non-Physiological Causes of Irritability - BOREDOM

- **Combating boredom in high school**
 - Advancing with her class
 - Doing teenager things
 - Getting out of the house
- **Combating boredom after high school**
 - Day programs
 - Companions

Camping on the Buffalo River!



Prom Night with Friends



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Longevity

Longevity in Rett Syndrome

- NIH-funded Rett Syndrome Natural History Survival Study
- '05-'06 collected information on 1928 females with RS and/or *MECP2* mutations
- Data analysis complete

Results of Survival Study

- **Survival in RS follows that of all females until age 10**
- **At age 50, survival in RS is slightly greater than 50% compared 95% in general population and compared to 27% of profoundly impaired persons**

WOMANHOOD...

Accentuate the *POSITIVE*

- **Scoliosis risk lessens**
- **Social skills and interaction improve**
- **“Rett Behaviors” diminish**
- **EEG may become more normal - seizures may occur less often or disappear**
- **Breathing irregularities may decrease**
- **Physical maturity is a NORMAL process**

UAB Rett Center Contact Information

1-800-822-2472, extension 7

Thanks!!!

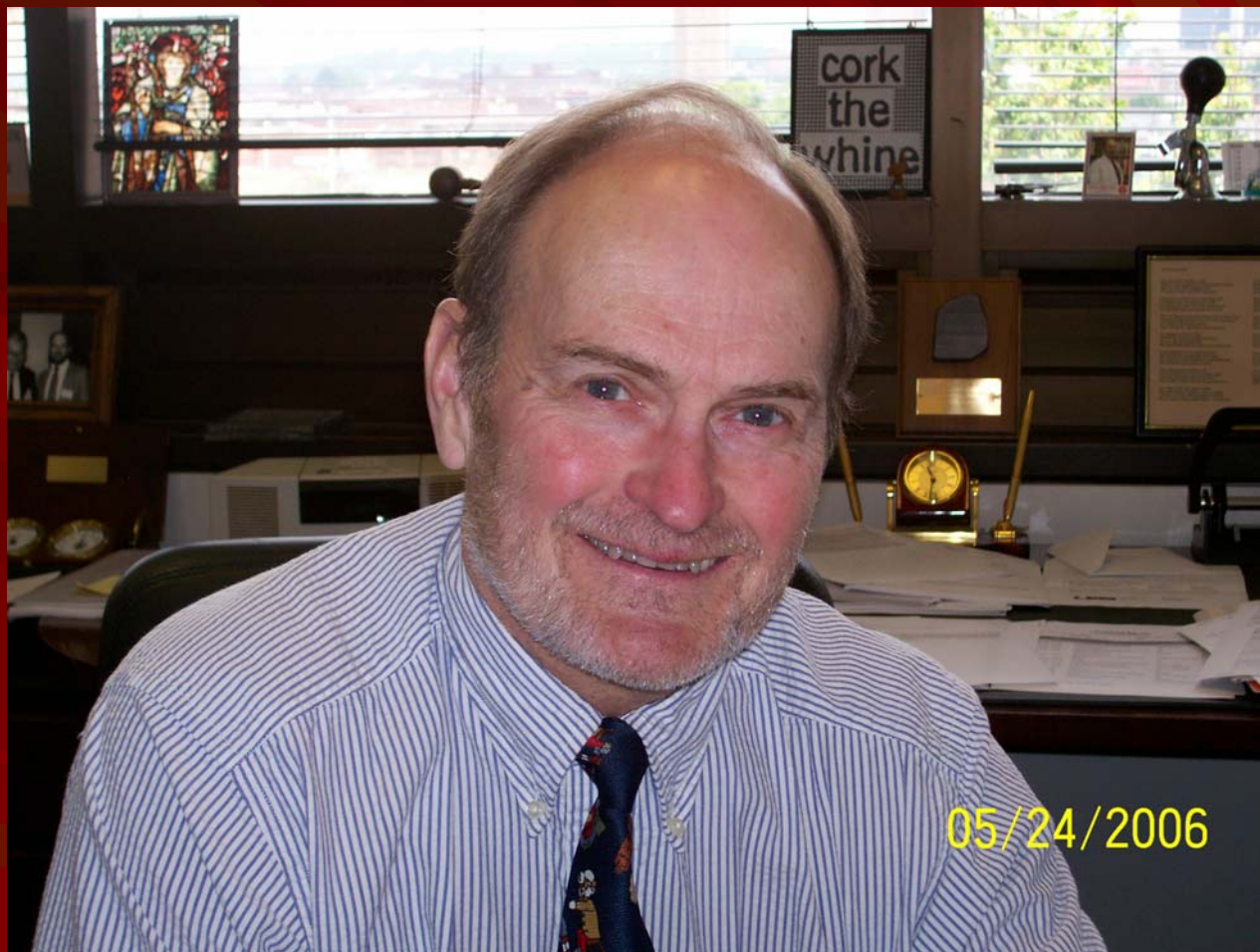
Jerry Childers



Suzanne Geerts, RD



Alan Percy, MD



And You

