Streams of Development and Behavior in XXY

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OBJECTIVES

1. Background of 47,XXY
2. Clinical Features of 47,XXY
3. Developmental and Behavioral profile
4. Syndrome-specific management

Prevalence compared to other syndromes

47, XXY	1 in 500
Down syndrome	1 in 700
Turner syndrome	1 in 2,500
Fragile X syndrome	1 in 4,000

Estimated rates of XXY diagnosis (1990-1993)

- Estimated babies born in region- 198,095
- Estimated number of males- 94,547
- Estimated number of 47,XXY males- 118
  - Prenatally– 10%
  - Postnatally- 26%
  - Undiagnosed- 64%

(Abramsky & Chapple, 1997)

Estimated XXY ages diagnosed postnatally

Diagnosed Under 1 year	Diagnosed 1-10 years	Diagnosed 11-20 years	Diagnosed More than 20 years
1%	0	7%	19%

Timing of Diagnosis of 47,XXY and 48,XXYY: A Survey of Parent Experiences

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- 47, XXY (n =89)
  - Developmental Concerns
    - First concern: 5.2 years (range 2 mo-20yr)
    - Age of diagnosis: 10 years (range 2 mo-30yr)
  - Endocrinologic issues
    - First concern: 19.1 yrs (range 3m-40y)
    - Age of diagnosis: 21.1 yrs (range 7m-40y)

AJMG, 2012

XXY Prevalence

- **Most common sex chromosomal disorder**
- **Prevalence of 1 : 581 males**
- **True incidence may be higher**
- **Many XXY males remain undiagnosed throughout their lifetimes:**
  - **No unusual physical features**
  - **Most with normal range of development**
  - **Chromosomal study not done routinely**

Hallmark of developmental milestones

- **Range of developmental milestones**
  - Range of normal is wide
    - Average age (e.g., sitting average age 6 months)
    - Average range (e.g., sitting average range 4-9 months)
  - Important to know what is within expected range
  - Make sure progressing appropriately
  - Not just achieving milestones but doing them correctly
    - No wide gait when walking
    - Speech is intelligible and spontaneous

Development of Children with XXY

- The developmental progress for a child with XXY
  - Wide range of individual differences in rates of development, especially in language
- How to help the child progress appropriately
  - Effective therapy and practical teaching strategies
  - Balancing family needs with the needs of the child

Interventional Therapies

- Key Points
  - May not qualify for services if within the "average range"
    - Continue to monitor (every 3-6 months)
    - Ask for home-based program
    - Private therapies
    - Use alternative strategies
      - » Swimming instead of physical therapy
      - » Joining boys scouts instead of social skills training

Interventional Therapies

- Key Points
  - Therapists provide guidance
  - Parents make it happens
    - Home practice program
    - Daily practice
    - Do 5 minutes activities throughout the day
    - Incorporate with daily activities
  - Teach the correct way early
  - Focus on long-term functional outcome

Principles of Typical Development

4 domains of function

- Gross motor (cephalocaudal progression) = physical therapy
- Fine motor (midline to periphery; proximal to distal) = occupational therapy
- Language = speech therapy
  - Expressive communication
  - Receptive communication
- Social-adaptive

Gross Motors

HEAD CONTROL > ROLL OVER
TRUNK CONTROL > SIT
HIP CONTROL > CRAWL
LEG CONTROL > WALK

Gross Motor Milestones

- Newborn
  - Reflex activity predominates
    (Moro, stepping, grasp reflexes)

Gross Motor Milestones

- 0-3 months: Reflex activity predominates. Development of head control
  - Prone
    - Newborn- Touches chin
    - 2 months- Lifts head and chest (45 degrees)
    - 4 months- Extends arms (90 degrees)
  -

Gross Motor Milestones

- Supine
  - 2 months- Head lag on pull to sit
  - 4 months- Head in plane with body on pull to sit, controlled in sitting
  - 6 months- Head leads in pull to sit

Gross Motor Milestones

- 0-3 months: Development of head control
  - Ventral suspension
    - 1 month- Lifts head to plane of body
    - 3 months- Lifts head above body, extends legs

Gross Motor Milestones

- 1-8 months: sitting
  - 1-2 months
    - No trunk control
    - Head unsteady
  - 2-3 months
    - Raises head and shoulders
    - No thoracolumbar control

Gross Motor Milestones

- 4 - 8 months: Rolling and sitting
  - 4 months
    - Rolls front to back
    - Sits with support (head steady)
    - Lumbar area control
    - Good head control
  - 5 months
    - Rolls back to front (supine to prone)

Gross Motor Milestones

- 4 - 8 months: Rolling and sitting
  - 6 months
    - Sits alone, props on hands
  - 8 months
    - Gets into sitting position

Gross Motor Milestones

- 9-12 months: Creeping and walking
  - 9 months
    - Crawls
    - Pulls to stand

Gross Motor Milestones

- 9-12 months: Creeping and walking
  - 10 months
    - Cruises
    - Walks with two hands held
  - 12 months
    - May walk alone (9-17 months)

Gross Motor Milestones

- 18-24 months: Running and climbing stairs
  - 18 months
    - Runs clumsily, walks pull/push toys
    - Walks up/down stairs with one hand held
  - 24 months
    - Runs well (wide-based gait)
    - Walks up/down stairs alone

Gross Motor Milestones

- 3-4 years: Alternating leg movement
  - 3 years
    - Peddles tricycles
    - Balance on one foot for 1 sec
  - 48 months
    - Walks on tiptoes

Gross Motor Milestones

- 2-6 years: Balance and Coordination
  - 2 years
    - Kicks ball forward
  - 3 years
    - Hops 2-3 times
  - 4 years
    - Skips
  - 5 years
    - Jumps rope

XXY : Gross Motor Development

- **Spectrum of development and behavior**
  - **Some boys may not have gross motor delays**
  - **Some boys more affected than others**
  - **Possibly influenced by age of diagnosis, therapies, etc…**
- **Delayed and/or uncoordinated motor skills**
- **Decreased tone, strength, and coordination**

Gross Motor and Growth

- **Infancy**
  - Hypotonia, especially upper trunk
    - **late walking (most walk by 12 mo with tx; 18 mo without tx)**
  - Normal height
- **Childhood**
  - Increasing height, usually between ages 5-8 years
- **Adolescence**
  - Decreased upper to lower body segment ratio
  - Increased armspan
  - Narrow shoulder (2cm decrease) and wide hips (1 cm increase)

47, XXY: Physical Features

- **Tall stature**
  - **Increase in height significant between ages 5 and 8**
  - **Mean final height**
    - **XXY: 6 feet**
    - **XYY: 6 ft 3 in**
  - **5 inches taller than father**

Bones and Joints

- Flat Feet
  - Pes Planus
  - Treatment controversial in mild cases
    - Arch supports vs. no arch supports
  - Moderate to severe cases
    - Orthopedic Evaluation
    - Orthotics

Increase likelihood for…

- Delayed gross motor development
  - Physical Therapy
- Poor tone, coordination, and strength
  - Extracurricular activities (e.g., swimming, horseback riding, running, hiking, walking up/down hill)
- Unable to keep up with peers in sport activities
  - Seek other non-sport activities your son may be interested (e.g., art, music, computers, hiking)

Fine Motor (Visual Motor) Milestones

- 0-3 months: Gross movements dominate. Development of tracking
  - 0-2 months
    - Primitive grasp
    - Keeps hands fisted
  - Emergence of Asymmetric tonic neck reflex (ATNR): fencing posture
    - appears at 2 weeks
    - disappears at 2-3 months

Fine Motor (Visual Motor) Milestones

- 0-3 months: Gross movements dominate. Development of tracking
  - 1 month
    - Follows to midline
  - 2 months
    - Follows past midline
    - Fixes and follows
  - 3 months
    - Hands open, regards hands

Fine Motor (Visual Motor) Milestones

- 4-6 months: Emergence of hand use
  - 4 months
    - Midline hand play
    - Reaches for objects
    - Grasps rattle
    - Brings objects to mouth

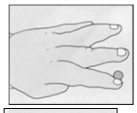
- .
- .

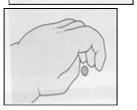
Fine Motor (Visual Motor) Milestones

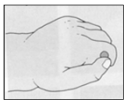
- 4-6 months: Emergence of hand use
  - 6 months
    - Reaches with either hand
    - Rakes objects, palmar grasp
    - Transfers objects
    - Plays with toes

Fine Motor (Visual Motor) Milestones

- Grasp Development/voluntary release
  - 6 months
    Rake, takes one cube only
  - 7 months
    Radial-palmer grasp
  - 8 months
    scissor grasp, takes 2 cubes (one in each hand, bangs cubes together)

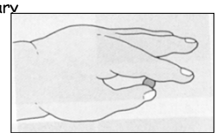






Fine Motor (Visual Motor) Milestones

- Grasp Development/voluntary release
  - 9 months
    Inferior-pincer grasp (immature pincer)
  - 12 months
    Fine-pincer, grasp using fingertips



Fine Motor (Visual Motor) Milestones

- Tower and complex control
  - 15 months
    Tower of 2 blocks (vertical before horizontal)
  - 18 months
    - Tower of 3-4 blocks
    - Turns pages 2-3 at a times
    - Scribble
    - Uses Spoon for solids

Fine Motor (Visual Motor) Milestones

- 3-6 years- Copying and building skills
  - 3 years
    - Copies circle
    - Uses scissors
    - Uses spoon/fork
    - Draws head without a body
  - 4 years
    - Copies cross
    - Draws person with 3-4 body parts
  - 5 years
    - Ties shoelace, print letters

Bones and Joints

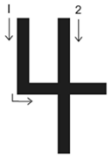
- Elbows
  - Radioulnar synostosis
  - Inability to pronate and supinate forearm
  - Limited range of motion can interfere with fine motor skills (e.g, handwriting, posture, school successes)
  - X-ray if limited range of motion
  - But, usually no treatment…

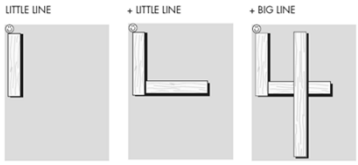
Therapies Considerations for Fine Motor

- Occupational Therapy
- Handwriting program
  - Handwriting without tears
    - www.hwtears.com
- Computers
- Musical instrument
- Practical practice strategies
  - Tie shoes, button, color, draw
- Inform school
  - Extra time to complete task

Handwriting

- Handwriting Without Tears
  http://www.hwtears.com/





Pencils for little hands

www.hwtears.com

Language Milestones

- 1 month
  - *Receptive*
    - Alerts to sound and voice
    - Shows social interest in faces and people
  - *Expressive*
    - Cries
- 2 months
  - *Receptive*
    - Smiles in response to being talked to
    - Shows social interest
  - *Expressive*
    - Coos (musical sounds), single vowel

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Language Milestones

- 4 months
  - *Expressive*
    - Reciprocal cooing and turn-taking
- 6 months
  - *Expressive*
    - Babbling (uses repetitive consonant/vowel sounds)
    - Imitate speech sounds like coughing, tongue clicking
- 9 months
  - *Receptive*
    - Understands approx 10 words
  - *Expressive*
    - Says "dada" and "mama" nonspecifically
    - Sing-song jabbering of babbling sounds

Language Milestones

- 12 months
  - *Expressive*
    - Says "dada" and "mama" specifically
    - Produces single words
      (9 - 12 months)
    - Points for needs and for interesting objects or actions
    - Gestures
    - Creates complicated babbling called jargon which sounds like sentences

Language Progression

Expressive

- 15 months
  - 4-6 words
- 18 months
  - 7-25 words

2-6 years: Word combination

Expressive

- 24 months
  - 50+ words
  - combine 2 words together
- 36 months
  - 250+ words
  - 3+ word sentences
  - Pronouns, plurals, future tenses
  - Count 3 items

2-6 years: Word combination

Expressive

- 4 years
  - 5-6 word sentences
  - Name 3-4 colors
  - Count 5-10
  - Past tenses
  - Ask questions
- 5 years
  - Uses all parts of speech
  - Knows past, present, future
  - Count to 10

Speech Intelligibility to Strangers

-2 years	50%
-3 years	75%
-4 years	100%

Language Milestones

- 4-9 months
  - *Receptive*
    - Deliberately turns head toward sound
    - Responds appropriately to tone of voice
    - Responds to name
- 9-12 months
  - *Receptive*
    - Comprehends verbal routines, such as "wave bye-bye"
    - Responds appropriately to "no"
    - Understands pointing
    - By 12 month, obeys commands with gestures with rapid growth in receptive language

Language Milestones

- 15 months
  - *Receptive*
    - Follows one step command without gestures
    - Finds 1 body part
- 18 months
  - *Receptive*
    - Understands at least 50 words
    - Find 5 body parts
    - Points to 1-2 pictures

Language Milestones

- 24 months
  - *Receptive*
    - Follows 2 step commands
    - Points to named pictures
- 36 months
  - *Receptive*
    - Understands 2 prepositions
    - Knows first/last name
- 48 months
  - *Receptive*
    - Understands opposites (big/small)
    - Tells stories

47, XXY: Linguistic function

- **Speech delay evident by 12 month of age**
  - **Delayed vocal plays / ability to produce sounds**
  - **First words spoken at 18 -24 months**
- **24 months of age: expressive language worse than receptive language = *verbal apraxia***
- **Pre-school years**
  - **Shy when language demands high**
  - **"Tip of the tongue" phenomenon**
    - **Speech on command difficult**
    - **Difficulty formulating sentences and expressing thoughts**

47, XXY: Linguistic function

Consequences of language deficits:

- **Lower verbal IQ than performance IQ**
  - **Denver study: VIQ 94 and PIQ 99**
  - **Boston study: VIQ 95 and PIQ 110**
- **50% with dyslexia**
- **Increased risk for reading and spelling impairment**
- **Inability to cope with social situations--passive, social withdrawal, frustrations, outbursts**

Consequences of language deficits

AT RISK FOR:

- Short attention span
- Impulsivity
- Social Skills problems
- Sensory Integration Problems
- Anxiety, Depression, Mood Disorders

47, XXY: Linguistic function

- **Deficits in verbal skills may persist into adulthood**
  - **10 to 20 points reduction in verbal skills in adolescence *(Ratcliffe and Paul, 1986)* and adulthood *(Netley, 1986)***
  - **Cases of older males with verbal skills better than performance skills *(Boone-Brawer, 2006)***
  - **50 males with XXY (4.1-17.8 years), impairment in both verbal and non-verbal cognition *(Ross, 2008)***
    - **Older group- impaired language/motor function**
    - **Younger group- attention problems**

Action Plan

- **Speech therapy (focus on pragmatics)**
- **Social skills training**
- **School accomodations**
  - **Small group settings within classroom**
  - **Prompt answers**
  - **Praises**
- **Practical strategies**
  - **Sitting in front of class**
  - **Play date with peers**

Language Development

- **Pre-speech**- movement of muscle of face (ie- lip, jaw) and oral area (ie- tongue)
- Best practices- tone, strength, coordination
  - Blowing bubbles, horns
  - Mirror work
  - Sipping from straw
- www.talktools.net

Language Development

- Total communication- Speech therapy
- Non-verbal
  - www.signingtime.com
    -Signs do not replace speech, but encourage its development
    -Hand over hand teaching of these signs to learn how to use them
  - Gestures, pointing, etc..
  - Pictures
- Verbal- focus on pragmatics
  - Reading books, singing
  - Play group

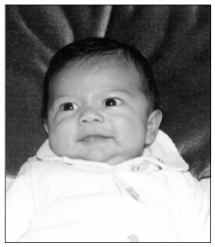
Picture Communication

- Pictures can promote language development
- Pictures can be traded for an object or pointed to as a request
- Pictures can be low tech (paper) or high tech (on a device)
- Works better with two people in the beginning

Picture cards

Social-Adaptive Milestones

- 0-3 months: Bonding
  - Newborn- recognizes mother's face
  - 6 weeks- social smile
  - 2 months- regards face



Social-Adaptive Milestones

- 4-8 months:
  - 4 months- laughs
  - 6-8 months- prefers primary caretaker, stranger anxiety, holds bottle, finger feeds

9-15 months: Social Interactions

- 9 months
  - Plays peek-a-boo, pat-a-cake
  - Uncovers hidden object
  - Waves bye-bye
  - Separation anxiety

12 months
Plays simple games
Interest in books

2-4 years: Play

- 2 years
  - Terrible two's
  - Parallel play
- 3 years
  - Cooperative play, takes turns, shares
  - Knows name, asks why, sense of humor
- 4 years
  - Prefers peer play
  - Tell stories

Aquatic Therapy

www.koolkidsfoundation.org

The water/pool is a great natural environment

- Indications
  - Trunk and extremity weakness
  - Decreased cardiovascular endurance/stamina
  - Decreased weight bearing status
  - Decreased motor control
  - Decreased attention to task

Hippotherapy

www.chastainhorsepark.org

Music therapy

www.mtsofga.com

"Therapy Moments"

- Getting dressed
- Snack
- Playing with the dog, cat
- Going to run an errand
- At the beach
- Playing sports
- Bathtub time
- Book reading
- Going to the bathroom/washing hands
- Watching TV

Key Points

- Play
  - All children learn through play from the time they are born
  - Help child learn what toys do and how to play with them
  - Show children how to get into imaginative play by joining in with activities
  - Imaginative games in second year of life are valuable learning opportunities

Key Points

- Structured Teaching
  - Try to provide the extra learning experiences within regular daily activities
  - Examples- reading books, drinking from a cup
  - Prompt child at each steps as necessary, so that they successfully complete the task
  - Child learn by imitation and practice rather than by trial and error

Key Points

- Practice
  - Increase the skill and efficiency of learned tasks
  - Examples- using a spoon/fork, dressing, dancing
  - As children progress year by year, improvement is influenced by amount of practice
  - Practice in different environment

Key Points

- Empower the child
  - Verbally praise your child (eg. "you are so smart")
- "Try again"
  - Using "try again" instead of "no" when the child does not do something correctly
  - Teach the correct ways early

Sensory Integration Dysfunction

- Difficulty processing information from the senses (touch, movement, smell, taste, vision, and hearing) and responding appropriately to that information.
- One or more senses that either over- or underreact to stimulation.
- Sensory processing disorder can cause problems with a child's development and behavior
  - Withdraw when touched.
  - Refuse to eat certain foods because of how the foods feel when chewed.
  - Oversensitive to odors.
  - Hypersensitive to certain clothes
  - Dislike getting his or her hands dirty.

XXY: Behavioral Features

- **Personalities variable**
  - **Friendly, helpful, relate well to people**
    (Leonard, 1991)
  - **Timid, immature, reserved, poor peer relationship**
    (Robinson, 1991; Ratcliff, 1982; Bancroft, 1982)
  - **Risk of psychiatric disorders – anxiety, depression, substance abuse**
    (Bender, 1995)

XXY: Social Development

- Prospective studies:
  - Not deliquents, criminals, arsonists, etc.
  - Shyness, social withdrawal common behavioral traits
- New studies: Netherlands
  - Social Cognitive deficits in adults
    - Van Rijn, 2006 & 2008
    - Distress is social interactions
    - Less engagement in social behaviors and activities
    - Higher ratings on autism rating scales
  - Autism spectrum disorders
    - Bruining, *Pediatrics*, May 2009
    - Age 6-19, n=53, recruited through Dutch Klinefelter Assoc.
    - 27% with autism spectrum disorders

47, XXY Behavioral Features

- **Social deficits may persist into adulthood**
  - **Males with XXY (mean age 39.2 years) compared to XY males (mean age 35.7 years)**
    - **Males with XXY reported less often engage in social behaviors associated with negative emotions**
      - ***Refusing a request or standing up for one's rights***
    - **Adults with XXY have deficits in social-emotional cues with increased levels of emotional arousal**
      - **Less able to identify and verbalize their emotion**

(van Rinj, 2006 and van Rinj, 2008)

The psychosocial impact of Klinefelter syndrome and factors influencing quality of life

Amy S. Herlihy, BSc[1,2,3,4], Robert I. McLachlan, MD, PhD[1,3,4], Lynn Gillam, MA, PhD[5,6], Megan L. Cock, BSc, PhD[4], Veronica Collins, MSc, PhD[1,7], and Jane L. Halliday, BSc, PhD[1,7]

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Table 2 Characteristics of study participants

Participant characteristics	*N* (%)
Total	87 (100)
Age at study	
18–29 yr	16 (18)
30–49 yr	46 (53)
50 yr and older	25 (29)
Education level	
Did not complete high school	30 (34)
Completed high school	48 (55)
Further than high school	9 (10)

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Table 5 Comparison of outcome measures between study population and population normative means

Measure	*N* (%)	Study population	General population
Personal Wellbeing Index (PWI)			
Subjective well-being (mean ± SD)	87 (100)	61.7 ± 24.6	76.1 ± 12.5[a]
Satisfaction with life as a whole (mean ± SD)	86 (99)	60.6 ± 28.6	78.5 ± 16.6[a]
Body image (MBSRQ-AS)			
Appearance evaluation (mean ± SD)	87 (100)	2.9 ± 0.8	3.5 ± 0.8[a]
Appearance orientation (mean ± SD)	87 (100)	2.8 ± 0.7	3.6 ± 0.7[a]
Self-esteem (RSE)			
Score (mean ± SD)	86 (99)	19.1 ± 7.1	31.6 ± 5.1[a]
Psychological distress (K10)			
High/very high	86 (99)	43%	10%[a]
Health status (SF1)			
Poor/fair	86 (99)	34%	15%[a]
Body mass index (BMI)			
Overweight/obese (BMI of ≥25)	79 (91)	67%	56%[a]

N refers to the number of participants who answered the question. All measures were significantly different between the two groups ($P < 0.001$).
MBSRQ-AS, Multidimensional Body-Self Relations Questionnaire-Appearance Scales; RSE, Rosenberg Self-Esteem Scale.

Study Results

- **Psychosocial factors:**
  well-being, self-esteem, body image, mental health, general health
- **XXY participants lower compared to general male population**
- **Age of diagnosis not a major predictor of psychosocial outcomes in adulthood**
- **Better psychosocial outcomes: employment status, social support, physical features**

Key Points for Social Development

- Goal- Enhance self-esteem
  - Social skills training
  - Social Stories
  - Hobby and interest
  - A few trusted close friends
    - Play dates
  - Teach socially age-appropriate behavior early
    - A 10 y/o should not sit on parents lap in social setting
- Teach appropriate behavior for private vs. public setting

Medication Consideration

- Medications for psychological or behavioral problems
- Not everyone will need medications
- Medication treatment should always accompany behavioral therapies
- Criteria for medications: (Only 1 needed)
  - Child expresses distress
  - Interferes with learning, academics progress
  - Interferes with social development
  - Interferes with overall home life/general functioning

Questions?