Autism: Overview, Treatment, and Communication

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Disclosures

No conflicts to disclose
Learning Objectives

Pharmacists and technicians:
- Describe the criteria used to diagnose autism
- Identify common comorbidities for autism
- Evaluate the effectiveness of their communication with a person with autism

Pharmacists:
- Recommend and monitor pharmacological treatment for autism and its comorbidities
Autism and Pharmacists

Pharmacy school may not cover the disorder

Not enough specialists—psychiatrists

Primary care managing patients

Higher frequency of adverse effects

Patients’ and caregivers’ frustrations with their providers

Incredible time commitment and confusion
Outline

Diagnosis criteria
Epidemiology
Etiology
Pathophysiology
Pharmacotherapy
Communicating with autism patients and their families
Autism Spectrum Disorder (ASD)

- Developmental disorder characterized by social, communication, and behavioral challenges
- Signs often noticed early in life but diagnosis can be delayed
- Generally life-long disorder
- Formerly known as
  - Autistic syndrome
  - Asperger disorder
  - Pervasive developmental disorder not otherwise specified
Diagnosis
Diagnosing

No laboratory tests
Evaluate behavior and history
Trained professionals can diagnose by age 2
Symptoms often noticed younger
Understanding the definition is important for the healthcare team

Diagnosis includes 4 required sections
- Deficits in social communication interactions
- Restricted, repetitive behavior, interests, or activities
- Present in early development, but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life
- Cause clinically significant impairment in functioning

Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. APA, 2013
Diagnosis part 1: Deficits in Social Communication Interactions

3 out of 3 required deficits
- Social-emotional reciprocity
- Non-verbal communication
- Developing, maintaining, and understanding relationships

What this looks like: #nofilter
- Taking turns in conversations
- Not understanding unspoken messages
- Not understanding layered levels of relationships
- Perspective-taking
- Peer pressure

Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. APA, 2013
Diagnosis part 2:
Restricted, repetitive behavior, interests, or activities

2 out of 4 required for diagnosis
- Stereotyped or repetitive motor movements, use of objects, speech
- Insistence on sameness/ritualized behavior
- Restricted, fixated interests
- Hypo-hyperreactive to sensory input

What this looks like: #nofilter
- Difficulty with transitions
- Stimming
- Lining up toys
- Single topic of conversation
- Great with routines, and patterns
- Sensory overload & meltdowns

Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. APA, 2013
Diagnosis parts 3 and 4

Part 3
- Present in early development, but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life

Part 4
- Cause clinically significant impairment in functioning

Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. APA, 2013
Diagnosis:
Severity for parts 1 and 2

Level 1
  ◦ Requiring support

Level 2
  ◦ Requiring substantial support

Level 3
  ◦ Requiring very substantial support

Diagnostic and Statistical Manual of Mental Disorders, 5th Ed. APA, 2013
Severity vs Spectrum

**MEASURED INTELLIGENCE**
- Intellectual disability — Gifted

**SOCIAL INTERACTION**
(Making eye contact, enjoying interaction with others, etc.)
- Not interested in others — A variety of friendships

**COMMUNICATION**
(Using words correctly to communicate)
- Nonverbal — Verbal

**BEHAVIORS**
(Repetitive behaviors, unusual behaviors such as hand flapping, etc.)
- Intense — Mild

**SENSORY**
(Response to touch, smell, sound, taste, and feel)
- Not very sensitive — Very sensitive
- Pain
- Sounds

**MOTOR**
(Gross motor, such as walking)
(Fine motor, such as using fingers to grasp a small item)
- Uncoordinated — Coordinated
- Fine
- Gross

[www.cdc.gov/ncbddd/autism/signs.html](http://www.cdc.gov/ncbddd/autism/signs.html)
Severity vs Spectrum:
The patient’s perspective

Sometimes when people think of this word, they think of the autism spectrum as being like this:

A very linear looking ‘spectrum’, which gives the impression that people range from being ‘a little autistic’ to ‘very autistic’.

Hm. How can you be ‘a little autistic’?

It’s that vague language that I always find confusing.

https://the-art-of-autism.com/understanding-the-spectrum-a-comic-strip-explanation/
Severity vs Spectrum:
The patient’s perspective

The spectrum consists of many different ‘traits’, or ways in which the brain processes information.

Some traits create difficulties in everyday life.
(hence being diagnosed)

But also many traits are useful in everyday life.

https://the-art-of-autism.com/understanding-the-spectrum-a-comic-strip-explanation/
Epidemiology

WHO IS MOST AFFECTED
Child Prevalence

8-year-old children

325,483

8% total population

www.cdc.gov/ncbddd/autism/addm.html
Child Prevalence

1.7% is the average percentage identified with ASD

1 in 59 8-year-old children were identified with ASD by ADDM in 2014

www.cdc.gov/ncbddd/autism/addm-community-report/key-findings.html
ADDMM
Prevalence over time

Baio J et al. MMWR Surveill Summ. 2018; 67(SS-6): 1-23
ADDM key findings

Gender Ratio

Intellectual Ability

IQ less than or equal to 70
31%

IQ greater than 70
69%
...and 30% had not been recognized by their community provider by age 8
Adult prevalence

Fewer studies

Estimated similar to children

Adults more likely to have severe disabilities

For those no longer autistic, high rates of comorbidities
Pharmacist prevalence?
Comorbidities*

Medical
- Seizures
- Gastrointestinal issues
  - Malnutrition
  - Obesity
  - Constipation
- Asthma
- Allergies
- Bone fractures
- Pneumonia
- Down’s syndrome

Psychiatric
- *But are they really
- Sleep disorders
- Irritability (communication)
- Hyperactivity
- Anxiety
- Depression
- Obsessive-compulsive disorder

Lord C et al. *Lancet.* 2018 published online
Clinical issues

Gender identity
Transition to adulthood
Suicide risk
Patient vs caregiver goals
Blood draws for anything
Time burden/commitment
Insurance coverage
Access to services
Neurodiversity

Autism is part of the normal diversity of human brains

Humanity has benefited from contributions of people with autism

Many communicate very well, especially in writing

Frustration with a lack of voice in their care

Neurodiversity movement may be biased toward high-functioning, average IQ

- Typical presentation
- Drowns out voices of low functioning patients and families who need more care
Etiology
Risk factors

Maternal environment
- Nutrition
- Medication
  - Valproic acid
  - Opioids prior to conception
- Pesticides
- Parental age

Birth circumstances
- Low birthweight
- Preterm birth

MMR vaccine
- No

Genetics

Identified genetic causes
- Not clearly identified
- Fragile X

Heritability
- 70-93%

Older sibling with autism
- 7%-20% of subsequent siblings

Pathophysiology
## Neurobiology

### Brain volume
- Overgrowth early in development
- Altered connectivity
  - Over-all under-connectivity
  - Over-connectivity in specific regions (especially frontal and occipital lobe)
- Reduced/impaired growth later in development

### GABA signaling/switch

<table>
<thead>
<tr>
<th>Lobe</th>
<th>Normal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>Personality, behavior, emotions</td>
</tr>
<tr>
<td></td>
<td>Judgment, planning, problem solving</td>
</tr>
<tr>
<td></td>
<td>Speech: movement and writing (Broca’s area)</td>
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<tr>
<td></td>
<td>Body movement (motor strip)</td>
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<tr>
<td></td>
<td>Intelligence: concentration, self-awareness</td>
</tr>
<tr>
<td>Occipital</td>
<td>Vision (Color, light, movement)</td>
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<tr>
<td>Parietal</td>
<td>Interprets language, words</td>
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<tr>
<td></td>
<td>Sense of touch, pain, temperature</td>
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<tr>
<td></td>
<td>Interprets vision, hearing, motor, memory</td>
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<tr>
<td></td>
<td>Spatial and visual perception</td>
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<tr>
<td>Temporal</td>
<td>Understanding language (Wernicke’s area)</td>
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<tr>
<td></td>
<td>Memory</td>
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<tr>
<td></td>
<td>Hearing</td>
</tr>
<tr>
<td></td>
<td>Sequencing and organization</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>Balance, coordination, posture</td>
</tr>
<tr>
<td>Brainstem</td>
<td>Autonomic functions: breathing, heart rate, temperature,</td>
</tr>
<tr>
<td></td>
<td>wake and sleep cycles, digestion, sneezing, coughing,</td>
</tr>
<tr>
<td></td>
<td>vomiting, swallowing</td>
</tr>
</tbody>
</table>

Ben-Ari Y. *Trends in Neurosciences*. 2017;40(9), 536-554
Courchesne E et al. *Brain Res*. 2010;1380:138-45
Zielinski BA et al. *Brain*. 2014; 137 (6); 1799-812.
Treatment
Guideline recommendations

Screening
- No recommendation from US Preventative Services Task Force
- Recommended by most other authorities

Prevention
- Folic acid
- Vitamin D

Treatment
- Largely parent training or therapy interventions
  - Coaching parents and caregivers on how to interact with children with autism
  - School-based interventions
  - Equine or guinea pig therapy
- No first line drug therapy
- May use medications for comorbidities if necessary
Choosing medication treatment

Know what the actual diagnosis is

Define the goals of therapy

Use a validated tool to measure the progress toward goal

Use evidence, but be aware of the limitations of evidence in this population

Be suspicious of adverse reactions, including paradoxical

Treatment overview

**Irritability and aggression**
- Risperidone
- Aripiprazole
- Valproate*

**Stereotypy**
- Haloperidol *

**ADHD**
- Methylphenidate
- Atomoxetine
- Clonidine*
- Guanfacine*
- Naltrexone*

**Depression/anxiety**
- Children: Few studies
- Adults: possibly SSRIs

**Sleep disorders**
- Melatonin
- Awareness of transitions

**Core symptoms?**
- Bumetanide
- Folinic acid
- Buspirone*
- Olanzapine*
- Vitamin D3*

* = single study or mixed evidence

Goel R et al. Int Rev Psychiatry. 2018; 30(1);78-95.
Treatment:
Irritability and aggression

Risperidone

Aripiprazole
Treatment: Irritability and aggression

Risperidone and aripiprazole
- FDA approval: irritability associated with autistic disorder in pediatric patients
- For tantrums, self-injurious or violent behavior
- Reserve for those who are at risk for serious adverse events
- Best for stabilization—label indicates to increase dose to therapeutic effect, then titrate downward to reduce adverse events
- Head to head trial: neither superior to the other
<table>
<thead>
<tr>
<th></th>
<th>Ages</th>
<th>Initial</th>
<th>Recommended</th>
<th>Maximum</th>
<th>Dose</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aripiprazole</strong></td>
<td>6-17</td>
<td>2 mg/day</td>
<td>5-10 mg/day</td>
<td>15 mg/day</td>
<td>≤5 mg/day</td>
<td>≥1 week</td>
</tr>
<tr>
<td><strong>Risperidone</strong></td>
<td>&lt;20kg</td>
<td>0.25 mg/day</td>
<td>0.5 mg/day</td>
<td>3 mg/day</td>
<td>0.25 mg/day</td>
<td>Initial: 4 days</td>
</tr>
<tr>
<td></td>
<td>5-16</td>
<td>0.5 mg/day</td>
<td>1 mg/day</td>
<td>3 mg/day</td>
<td>0.5 mg/day</td>
<td>Subsequent: ≥2 weeks</td>
</tr>
</tbody>
</table>
Aripiprazole & Risperidone

Prolactin levels
- Risperidone increased
- Aripiprazole decreased

May dose either once daily, but twice daily may decrease somnolence

Side effects: weight gain, somnolence, anticholinergic, vomiting, constipation, EPS (not akathisia)

Lowers seizure threshold

Check for dose adjustments for CYP3A4 and CYP2D6 drug interactions and genetic tests
- Fluoxetine, paroxetine, carbamazepine

Possible Risk of TdP
These drugs can cause QT prolongation **BUT** currently lack evidence for a risk of TdP when taken as recommended.
Treatment:  
Core symptoms

FOLINIC ACID  
BUMETANIDE
Bumetanide for core symptoms
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Treatment</th>
<th>CARS</th>
<th>CGI</th>
<th>ADOS</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lemonnier et al (2012)</td>
<td>prospective, randomized, controlled</td>
<td>n = 60; Age 3-11 years; ICD-10 ASD</td>
<td>B 0.5 mg bid, n = 27</td>
<td>41.6 ± 3.6&lt;sup&gt;DO&lt;/sup&gt; 36 ± 5.7&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-E: 2.04 ± 0.87 51.8%</td>
<td>7.8 ± 7.4</td>
<td>Bed-wetting, n = 1; Hypokalemia, n = 7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo, n = 27</td>
<td>41.1 ± 4.1&lt;sup&gt;DO&lt;/sup&gt; 39.3 ± 4.9&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-E: 1.56 ± 0.85</td>
<td>5.3 ± 6.6</td>
<td>Bed-wetting, n = 1</td>
</tr>
<tr>
<td>Du et al (2015)</td>
<td>prospective, randomized, open-label trial</td>
<td>n = 60; Age 2.5-6.5 years; ICD-10 autism</td>
<td>B 0.5 mg bid and ABA, n = 28</td>
<td>36.39 ± 3.85&lt;sup&gt;DO&lt;/sup&gt; 30.79 ± 2.45&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-S: 3.17 ± 0.38 3.11 ± 0.39 1.89 ± 0.39</td>
<td>75.61 ± 11.38&lt;sup&gt;DO&lt;/sup&gt; 57.47 ± 7.19&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>Polyuria, n = 1</td>
</tr>
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<td></td>
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<td>ABA control, n = 32</td>
<td>37.28 ± 3.53&lt;sup&gt;DO&lt;/sup&gt; 31.64 ± 1.72&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-S: 3.4 ± 0.50</td>
<td>74.68 ± 4.47&lt;sup&gt;DO&lt;/sup&gt; 62.88 ± 4.96&lt;sup&gt;DO&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Lemonnier et al (2017)</td>
<td>prospective, randomized controlled</td>
<td>n = 88; Age 2-18 years; ICD-10 ASD</td>
<td>B 2 mg bid, n = 22</td>
<td>41.30 ± 5.44&lt;sup&gt;DO&lt;/sup&gt; 38.14 ± 6.19&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-I: 43.2%</td>
<td>106.58 ± 25.09&lt;sup&gt;DO&lt;/sup&gt; 87.03 ± 22.03&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>Hypokalemia, n = 16; Polyuria, n = 11; Anorexia, n = 9</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>B 1 mg bid, n = 23</td>
<td>41.43 ± 6.01&lt;sup&gt;DO&lt;/sup&gt; 38.04 ± 6.13&lt;sup&gt;DO&lt;/sup&gt;</td>
<td>CGI-I: 26.3%</td>
<td>106.42 ± 23.95&lt;sup&gt;DO&lt;/sup&gt; 87.96 ± 19.89&lt;sup&gt;DO&lt;/sup&gt;</td>
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</tbody>
</table>
| | | | B 0.5 mg bid, n = 20 | 42.45 ± 4.18<sup>DO</sup> 37.48 ± 5.59<sup>DO</sup> | CGI-I: 35.0% | 113.35 ± 17.48<sup>DO</sup> 100.9 ± 23.70<sup>DO</sup> |。
| | | | Placebo, n = 23 | 40.41 ± 4.89<sup>DO</sup> 38.78 ± 4.58<sup>DO</sup> | CGI-I: 4.8%; Kruskal Wallis: P = 0.004 | 112.68 ± 20.65<sup>DO</sup> 109.4 ± 26.07<sup>DO</sup> | |

Abbreviations: ABA, applied behavioral analysis; ABC, Autism Behavioral Checklist; ADOS, Autism Diagnostic Observation Schedule; ASD, autism spectrum disorder; B, bupenamide; C, control; CARS, Childhood Autism Rating Scale; CGI, Clinical Global Impressions Scale; CGI-E, Clinical Global Impressions Efficacy Index; CGI-I, Clinical Global Impressions Improvement Scale; GHI-S, Clinical Global Impressions Severity Scale; SRS, Social Responsiveness Scale.
Gamma aminobutyric acid (GABA)

- Allows chloride to enter the cell

**Normal action**
- Chief inhibitory neurotransmitter
- Normally chloride level within cell is low
- Hyperpolarizes cell = inhibits action potential

**Fetal neurons**
- Chloride levels high
- GABA is a stimulatory neurotransmitter
Paradoxical effects: Benzos and barbiturates in some epilepsy
Paradoxical effects: Benzos and barbiturates in some epilepsy

Effects of bumetanide on neurobehavioral function in children and adolescents with autism spectrum disorders

E Lemonnier, N Villeneuve, S Sonie, S Serret, A Rosier, M Roue, P Brosset, M Viellard, D Bernoux, S Rondeau, S Thummler, D Ravel and Y Ben-Ari
Bumetanide in autism 2017

Prospective, randomized, controlled

N=88; 2-18 years

Duration: 3 months

Intervention:
- Bumetanide 2 mg BID: n=22
- Bumetanide 1 mg BID, n=23
- Bumetanide 0.5 mg BID, n=23
- Placebo, n=23

Outcomes:
- Childhood Autism Rating Scale (CARS), Clinical Global Impressions Scale (CGI), Social Responsiveness Scale (SRS)
Bumetanide 2017 results
Bumetanide
2017 Potassium
Treatments:
Other conditions

Depression/anxiety
- SSRIs have not been studied in children, but poorly tolerated
- Adults: SSRIs better tolerated

Sleep disturbances
- Melatonin

ADHD/hyperactivity
- Methylphenidate
- Atomoxetine

Epilepsy

Dietary issues: constipation

Overall:
- Use guideline recommendations
- Monitor closely for adverse effects

Treatments:
Mixed, poor, or lacking evidence

N-acetylcysteine
Memantine
Donepezil
SSRIs for core symptoms
Lamotrigine
Levetiracetam
Clomipramine
Arbaclofen
Lithium

Oxcarbazepine
Topiramate
Oxytocin
Digestive enzymes
Sulforaphane
Omega-3 fatty acids

Goel R et al. Int Rev Psychiatry. 2018; 30(1);78-95.
Communication
Communication

Pharmacist-autism communication struggles
- Body language = rudeness
- Professional pride over communication mishaps
- Lack of training on autism
- Lack of time

Pharmacists are vital in autism
- Need medication, but higher rate of adverse effects
- Bridge the gap for primary care
- Non-psychiatric medications
- Be willing to be the expert
“Respect the way I need to communicate with you”: Healthcare experiences of adults on the autism spectrum

Christina Nicolaidis¹,²,³, Dora M Raymaker¹,³, Elesia Ashkenazy³, Katherine E McDonald³,⁴, Sebastian Dern³, Amelia EV Baggs³, Steven K Kapp³, Michael Weiner³,⁵,⁶ and W Cody Boisclair³
System-level Factors
- Availability of formal or informal supports
- Complexities of the healthcare system
- Accessibility of healthcare facilities
- Stigma about autism
- Other societal issues that affect health

Patient-level Factors
- Verbal communication skills
- Sensory sensitivities
- Challenges with body awareness
- Slow processing speed
- Atypical non-verbal communication
- Challenges with organization

Provider-level Factors
- Knowledge about autism in adults
- Incorrect assumptions about individual patients
- Willingness to allow written communication
- Use of accessible language
- Openness to providing other accommodations
- Skill in incorporating supporters

Success of Healthcare Interactions
Factors affecting experiences with healthcare

Autism-related
- Verbal communication skills
  - Literalness
  - Sensory sensitivities
  - Body awareness

Provider-level
- Lack of knowledge about autism
- Attributing all symptoms/behaviors to autism
- Equating communication to IQ
- Unwillingness to communicate in writing
- Skill in incorporating supporters

System-level
- Organization trouble in navigating system
- Stigma about autism
- Societal issues with employment/insurance
Recommendations from study participants to healthcare providers

“Respect the way I need to communicate with you”

Dim lights

Don’t use open-ended or vague questions

Find out how your patient’s needs are unique

Advocate for your patients

Information
  ◦ Navigating healthcare
  ◦ Aids to help prepare for interacting with providers
  ◦ Where to find good information
  ◦ Rights in healthcare
Tools for communication

Time

Remember the diagnosis
Review: Autism Spectrum Disorder Diagnosis

Deficits in social communication interactions (3/3 required)
- Social-emotional reciprocity
- Non-verbal communication
- Developing, maintaining, and understanding relationships

Restricted, repetitive behavior, interests, or activities (2/4 required)
- Stereotyped or repetitive motor movements, use of objects, speech
- Insistence on sameness/ritualized behavior
- Restricted, fixated interests
- Hypo-hyperreactive to sensory input

Present in early development, but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life

Cause clinically significant impairment in functioning
Tips for communication in autism

“Give me some space”

Turn down the noise and the lights

Listen for the message behind the behavior

Communicate your message clearly

Write or use pictures

Change your approach

Don’t use open-ended questions

Give choices to give control

Be patient.

Honor special interests

ocali.org/up_doc/Tips_for_Supporting_Individuals_with_ASD.pdf
Tips for communication in autism

“Give me some space”
Turn down the noise and the lights
Listen for the message behind the behavior
Communicate your message clearly
Write or use pictures
Change your approach
Don’t use open-ended questions
Give choices to give control
Be patient.
Honor special interests
Conclusion
Take home points

Autism diagnosis: impaired social communication; restrictive, repetitive behavior or interests

Prevalence is increasing, but services are struggling to keep pace

Medications are effective for comorbidities, but more likely to cause side effects

Communication requires time and keeping the diagnosis in mind
Autism

MALAURA CREAGER, PHARMD
NMPHA SPRING 2019

https://the-art-of-autism.com/understanding-the-spectrum-a-comic-strip-explanation/