UpToDate临床顾问
Official reprint from UpToDate®
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孤独症谱系障碍：临床特征

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我们的所有专题都会依据新发表的证据和同行评议过程而更新。

文献评审有效期至： 2021-10. | **专题最后更新日期：** 2021-08-02.

There is a newer version of this topic available in English. 该主题有一个新的英文版本。

引言

孤独症谱系障碍(autism spectrum disorder, ASD)是一种有生物学基础的神经发育障碍，表现为社会交流和社会互动的持久性缺陷，以及受限且重复的行为、兴趣和活动模式。

本文将总结ASD的临床特征。相关专题如下：

- (参见 "孤独症谱系障碍：初级保健中的监测与筛查")
- (参见 "孤独症谱系障碍：专业术语、流行病学和发病机制")
- (参见 "孤独症谱系障碍的评估和诊断")
- (参见 "儿童和青少年孤独症谱系障碍：治疗概述")
- (参见 "儿童与青少年孤独症谱系障碍的行为和教育干预")
- (参见 "儿童与青少年孤独症谱系障碍的药物干预")
- (参见 "儿童与青少年孤独症谱系障碍的补充和替代疗法")

术语

ASD的术语和诊断标准存在地区差异。(参见 "孤独症谱系障碍的评估和诊断"，关于'诊断标准'一节和 "孤独症谱系障碍：专业术语、流行病学和发病机制"，关于'专业术语'一节)

- 美国主要使用精神障碍诊断与统计手册第5版(Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, DSM-5)，其中采用“autism spectrum disorder”，即“孤独症谱系障碍”。

- 其他国家使用世界卫生组织国际疾病分类第10版(World Health Organization International Classification of Diseases, 10th revision, ICD-10)，其中采用“pervasive developmental disorder(PDD)”，即“广泛性发育障碍”[1]。2018年发布并开始准备实施的ICD-11[2]用ASD代替了PDD，但预计到2022年之后才会被成员国采用。

表型谱系和临床表现

ASD是一类异质性神经发育障碍，临床表现多样，主要是社会交流和互动缺陷，以及受限且重复的行为模式[3-5]，包括但不限于：

- 在2岁以内出现典型特征(表 1) [3,6-11]。

  约2/3的ASD患者在2岁之前未能习得交流技能。(参见 “孤独症谱系障碍：初级保健中的监测与筛查”，关于‘早期指示因素’一节)

- 社交技能在早期正常发育后出现停滞。

  约1/4-1/3的ASD儿童能够达到早期语言里程碑，但在15-24月龄时会出现语言、交流和/或社交技能倒退或停滞[4,12-16]。这种技能倒退可能逐渐出现，也可能突然出现，还可能出现在发育延迟或非典型发育之后[17]。

- 学前阶段对他人缺乏兴趣、缺乏同理心、语言或交流技能缺失或发育迟缓、明显抗拒变化且兴趣狭窄[18]。

- 若患儿表型较轻，父母或老师可能在其出现明显的社交技能缺陷(如，缺乏社会意识或社交能力)或语言技能缺陷之前，先注意到行为紊乱(如，过度关注自己喜欢的话题、组织能力不足或破坏性行为)或者与焦虑、注意缺陷/多动障碍(attention deficit hyperactivity disorder, ADHD)等共病相关的症状[19]。

社会交流和互动受损

社会交流是指与他人沟通想法、意图和情绪所需的言语及非言语技能[20]。成功的社会交流和互动需要下述多项技能和行为，它们相互之间存在重叠。

语言发育延迟和异常是ASD患儿父母最常见的主诉之一[21,22]。ASD患儿可能缺乏沟通和交际的意图，可能无法留意到、识别出和/或理解他人的社会交流行为[18]。(参见 “孤独症谱系障碍的评估和诊断”，关于‘诊断标准’一节)

社交情感互动

- **社会性注意**–是指用于社会互动的注意力、动机和行为[23]，包括观察、关注和思考他人以及试图与其建立社交连接，建立社交连接的方式有多种，包括目光接触和微笑、缩短距离、呼叫姓名或回应他人的社交行为(例如，回应他人的呼唤、使用语言或姿势、开始交谈)。

  ASD患儿的社会性注意行为的频率、持续时间和/或复杂程度都有限。他们还可能表现得不正常，例如[20,24,25]：

  - 对与其他儿童(包括兄弟姐妹)进行社会互动无兴趣或兴趣很低，仅在有需求时才与其互动。
  - 不模仿他人的拍手等动作。
  - 不对他人的社交行为做出恰当回应，例如，被他人呼唤姓名时不与其进行目光接触。
  - 与他人距离过近且未注意到这令他人感觉不适；对有社交动机的身体接触和感情表露持冷漠或厌恶态度。
  - 社会性注意行为异常或不协调(即使有社会动机)–例如，讲话时没有目光接触等非言语交流行为；另外，孤独症患儿可能会去推搡同伴来寻求社会性注意，但并没有开始交谈或做出其他更合适的社交行为。

- **共同注意**–也称“社会参照”，是指与社会同伴(例如，婴儿和照料者、幼儿和玩伴)分享兴趣或情绪(例如，快乐、成就或忧虑)的行为[26]，典型表现是：看看感兴趣的物品，再看看同伴的眼睛，目光在两者之间往复(通常在8-10月龄达到)；指向该物品(通常在14-16月龄达到)或将其展示给同伴[20]。

  ASD儿童通常延迟出现或缺乏共同注意，不会为他人展示、拿来或指出自己感兴趣的物品。虽然他们可能会指向自己想要的物品，但不会通过该动作与他人分享兴趣[27]。ASD幼儿可能满足于单独被动玩耍，常被其父母形容为不要求关注的“乖”孩子[28]。

非言语和语用交流行为

- **非言语交流**–ASD患者对眼神交流、面部表情、语调、手势、身体姿势及头部和身体朝向等非言语行为的使用及解读能力低下[29]。

  ASD患儿在与医生互动过程中可能回避目光接触、过于专注地凝视或盯住医生面部或除双眼之外的其他身体部位[30]。他们可能无表情变化，或做出夸张或“模式化”的表情；可能无手势交流或手势笨拙；讲话声音可能单调，缺乏情绪表达。

  ASD患儿也可能无法注意到他人的非言语交流，例如，未注意到社会同伴的面部，尤其是眼睛注视方向，无法理解社会同伴的兴趣和/或关注点。这些非言语交流障碍与上文提到的

社交情感互动障碍表现有所重叠。孤独症患者可能误解或无法理解他人的动作姿势(例如，指、挥手、点头或摇头)和表情。

- **语用交流**–是指在相应情境中成功运用语言所需的技能，包括遵循交流惯例(例如，按顺序发言、围绕话题讨论)，根据听者的需求调整语言(语言的复杂程度、话题选择)，通过变换语调改变句意，以及成功地使用非言语交流加深听者的理解。

  语用语言障碍是ASD的典型特征，可能伴有其他语言障碍。(参见下文'语言障碍')

  ASD患儿语用语言障碍的具体表现包括[24,29,31,32]：

  - 不将语言用作交流工具(例如，仅机械模仿他人的言语或对话)。
  - 难以开始或维持对话(例如，因为缺乏话轮转换或过分关注个人兴趣)。
  - 难以做出切题的答复和围绕话题进行交流，有时是因为缺乏眼神交流和无法正确理解谈话内容。
  - 无法顾及听者的兴趣、偏好和理解水平，无法向听者解释他们可能一无所知的话题。
  - 难以根据社交情境选择合适的言辞或话题(例如，言辞过于唐突，不考虑熟人和陌生人、正式和非正式场合的差别)。
  - 难以理解言语的含义(例如，做出与话题无关的应答)。
  - 不明白交谈情境或非言语交流如何改变言辞含义，因而难以领会隐喻、幽默、讽刺、戏弄、玩笑或欺骗(正常发育的儿童6-7岁时即可领会)[33-35]。

  虽然ASD患儿可学习语言的多重含义和社会性，但通常无法掌握其所有的微妙之处，难以将相关知识运用到实际中。他们学到非言语和语用交流技能(例如，讽刺或幽默)后，可能会不当使用(例如，对长者做出不当的讽刺性评论或开不合时宜的玩笑)，或将同伴的真诚评论误解为讽刺。

发展和维持友谊

- **社会认知**–需要在特定情境下捕捉、记忆、整合及解读社会信息和语言[36]，其包含社会性注意及非言语和语用语言技能的使用，这些均为成功社交和建立友谊所需。成功的社会认知需要在一定时间内多次观察、汇总所得信息以判断他人的想法、感受和意图。

  心智理论(theory of mind)属社会认知范畴，是指判断引发行为的精神状态(例如，信念、欲望、意图、想象和情绪)的能力[37,38]。具备该能力的人能够思考自己和他人的想法，例如，知道不同的人会有不同喜好、对同一事物的看法也有区别。由于一些ASD患儿的非社会性智力等认知领域正常，故一些学者认为心智理论缺陷是该病的关键特征[39,40]。

  社会认知障碍是ASD的核心特征，也是ASD与其他交流障碍原因的鉴别要点(表 2)。(参

见 “孤独症谱系障碍的评估和诊断”，关于‘鉴别诊断’一节)

社会认知障碍的具体表现包括：

- 不能正确理解他人的情绪反应(例如，误将他人的快乐理解为恐惧，无法理解他人的痛苦)
- 用大笑等不当方式回应他人的悲痛，这也可见于其他类型残障儿童
- 意识不到社会同伴对自己喜欢的话题不感兴趣
- 无法理解熟人、朋友和亲密关系的区别
- 难以判断他人的意图、信念、态度或可能的行为

虽然一些ASD患儿能成功理解特定情境下的社会信息，例如，看照片、读故事时，但他们可能无法识别或成功理解所有的社交情感行为，尤其是在现实中[41-43]。

- **社交互动和人际关系**–ASD患儿在社交情感互动、非言语和语用交流及社会认知方面存在缺陷，故难以建立和维持与儿童发育水平相符的同伴关系。

  ASD幼儿对发展人际关系的兴趣极低，他们可能更喜欢独自玩耍，可能仅将他人视为“工具”(即，借父母的手获取想要的物品，其间无眼神交流)[29]。他们可能较迟对主要照料者形成依恋。

  极少数ASD患儿会孤立到无法与亲爱的家人互动的地步。不过，同伴社交的频率和范围往往都有限。这可能是社交动机或兴趣有限造成的。此类儿童的父母可能将其表现称为“独立”而非“冷漠”，甚至可能为其表现出的自足而感到自豪。这些儿童可能也会社交，但不会像正常同龄人那样从中体验到欢乐和互惠[44]。有社交动机的ASD患儿也会进行有限社交，但他们无法改变社交行为以更好地满足社交需求，故社交不够成功，这可能为其带来显著痛苦。这类儿童无法获得满意的同伴关系，可能出现抑郁或遭受孤立、欺凌。

受限且重复的行为、兴趣和活动

ASD的另一核心症状是受限且重复的行为、活动和兴趣模式，以及对感官输入的敏感度过高或过低[29]。这些症状可能持续终生，在进入学龄期时尤其明显。(参见 “孤独症谱系障碍的评估和诊断”，关于‘诊断标准’一节)

刻板行为 — 刻板重复的运动性作态或复杂的全身动作(如，手或手指拍打或扭转、摇摆、晃动、倾斜、踮着脚尖走路)是ASD的核心症状之一[45-48]。ASD患儿可能刻板地将确切数量的玩具以同样的方式排列，而未明显意识到这些玩具代表着什么[44,49]。其他刻板行为包括延宕仿说(delayed echolalia)，例如重复自己在视频、电视节目或其他地方听到过的话语或奇怪短语[29]。

据报道，37%-95%的ASD患者存在运动性作态[50]。运动性作态常出现在学龄前期。刻板的运动性作态似乎是自我刺激行为，还可能自伤，例如，撞头、拍打脸/身体、咬或掐自己[26]。自伤行为在有重度智力障碍的ASD患者中更常见。刻板运动性作态或自伤行为的触发因素可能可预测(例如，挫败、焦虑、兴奋)或者看似随机。自伤行为可能是内部驱动的，也可能带有交流意图(例如，寻求关注、逃避、回避)。出现新发自伤行为时，应评估是否有疼痛、不适或感染等原因。

坚持同一性/抗拒改变 — 坚持同一性(认知僵化)是ASD的另一行为特征，这会干扰进食、交流和社交等功能活动，可能表现为当日常习惯发生微小改变时会感到痛苦(例如，发脾气、焦虑)，以及很难适应改变[29]。

患者在日常生活的各个方面可能遵循特定的非功能性常规或程序，例如：

- 总是按特定顺序吃特定食物
- 总是沿相同路线从一地到另一地
- 总是谈论同一事物或就特定话题重复询问
- 行为活动刻板(例如，逐字模仿在电视、视频或网站等处看到的内容)
- 无法忍受与“正常”或“期待”的行为方式产生偏差

这些行为与强迫症(obsessive-compulsive disorder, OCD)患儿类似，但与ASD患儿不同的是，OCD患儿通常能正常社交。(参见 “孤独症谱系障碍的评估和诊断”，关于‘鉴别诊断’一节)

兴趣狭窄 — 兴趣狭窄是ASD患者的另一特征[29]，具体表现包括：

- 对≥1种刻板或狭窄的兴趣模式过于关注，其强度或焦点不正常

  虽然许多幼儿兴趣狭窄，但ASD患儿的固着兴趣比正常发育儿童的兴趣更为特定、不寻常和强烈，他们常对火车、汽车等机械话题或自然科学话题感兴趣，即使受到多次提示、请求，也很难将注意力从自己喜欢的话题上移开。这会造成社交互动障碍，并使他们难以完成家务、功课或日常事务。

- 持续过于关注吊扇、吸尘器等不寻常物体

  幼儿可能过于迷恋独特的感觉或知觉刺激[26]。(参见下文‘异常感觉行为/异常感知’)

  年龄较大儿童和认知能力较强儿童可能过于关注：天气、日期、日程安排、电话号码、车牌号码、托马斯火车玩具、宠物小精灵(Pokémon)或任何类别中的亚型(如，恐龙、狗、飞机)[26,29]。

异常感觉行为/异常感知 — ASD患儿常有感知异常[50]，可能对噪声、接触、气味、口味或视觉刺激等环境刺激反应过度、不足或异常[51]。感知异常使其唤醒度升高，易出现疏忽、焦虑和/或发怒。

感知异常的具体表现包括[26,29]：

- 通过眼角去观察物体。
- 过于关注边缘、旋转物体、闪亮的表面、灯或气味。
- 拒绝或只吃某些味道/口感的食物。

  这可能导致体重异常、腹泻、便秘等胃肠道症状，这些症状在ASD患儿中的发生率似乎高于非ASD儿童[52-56]。这还可能造成挑食和营养缺乏[57-59]。

- 过于沉迷嗅或舔非食物性物体。
- 触觉防御或抗拒被触碰或对某些类型的触碰过于敏感；轻触可能使其痛苦，而深压却可能使其平静。可能包括抗拒某些质地或颜色的贴身衣物。
- 明显对疼痛漠视。
- 强烈偏好和/或强迫性触碰某些质地，而强烈厌恶其他质地。
- 对某些频率或类型的声音高度敏感(如，远处的消防车)，但对近处的声音或会吓着其他儿童的声音却没有反应。

伴随病症

ASD可能伴有其他病症，做出诊断时应明确指出有无这些情况[29]。

智力障碍 — ASD患者无论总体智力水平如何，其认知技能通常是不均衡的[29,60]。在需要死记硬背、机械性、视觉空间或知觉处理的任务方面的表现往往优于需要更高层次概念处理、推理、解读、整合或抽象思维的任务[60-63]。智力障碍参见其他专题。(参见 “儿童智力障碍的定义、诊断及需求评估”)

语言障碍 — 虽然ASD患儿常有语言障碍，但这并非诊断所必需的。诊断ASD时应明确指出有无语言障碍[29]。(参见 “儿童言语和语言障碍的病因学”和 “儿童言语和语言障碍的评估和治疗”)

如同ASD患儿的其他异质性表现，语言障碍的严重程度和性质也有很大差异。

伴有语言障碍的患儿可表现为：

- 不交流，即完全不与他人分享想法或兴趣，也不提要求
- 只用身体语言交流，即拉着成人的手以在其帮助下获取某些物品或进行某些活动，但没有口头和眼神交流
- 只说单个词汇或短语

- 语言发育迟缓

  大多数ASD患儿的感受性语言发育延迟程度远高于表达性语言。患儿可能对别人叫自己的名字没有回应，父母可能主诉担心患儿存在听力障碍[18,64]。

- 语言发育倒退

- 无法理解简单的问题或指示

- 说话的旋律、语气和语调变化异常，或节奏不均匀

不伴语言障碍的患儿(例如，能说出语法正确的句子)可能存在上述语用语言功能异常。(参见上文‘非言语和语用交流行为’)

其他神经发育障碍 — ASD常伴有其他神经发育障碍或其症状[65-71]。随着患儿经历负面社会经历和对自身差异及社交困难(例如，孤立、边缘化和欺凌)的认知增加，这些共病(例如，焦虑、ADHD、破坏性行为和抑郁)的症状可能加剧[72-74]。

与ASD相关的神经发育障碍有[68-70,75,76]：

- 焦虑障碍–ASD患者的焦虑发生率显著高于社区人群，焦虑障碍的患病率约为42%-55%，会造成一定程度损害的焦虑患病率则为11%-80%[73,77-79]。关于焦虑是孤独症的核心特征、ASD相关障碍引起的特征还是独立的伴随病症，目前尚存争议[80,81]。(参见 “儿童和青少年焦虑障碍：流行病学、发病机制、临床表现和病程”)

- ADHD–ASD患儿合并ADHD的比例为30%-50%[82-84]。(参见 “儿童和青少年注意缺陷/多动障碍的临床特征和诊断”，关于‘临床特征’一节)

- 对立违抗性障碍等破坏性行为障碍。

- 抑郁等心境障碍，更常见于青少年和成人，尤其是无智力障碍者[79,85,86]。

- 抽动障碍。(参见 “儿童多动性运动障碍”，关于‘抽动障碍’一节)

- 学习障碍–无智力障碍的ASD患儿即使标准化测验成绩不错，也可能存在学习障碍。他们可能在3、4年级开始出现学习障碍，在该阶段语用语言技能和社会认知能力的不足会影响阅读理解和书写表达。执行功能障碍也常影响该阶段及之后的学业。若ASD患儿的学习障碍未被发现及干预，其可能产生挫败感并出现问题行为。

  学习障碍的具体表现包括：

  - 在与自己兴趣无关的主题方面表现不佳

  - 小组学习或课堂讨论时表现不佳

  - 需要自主管理日程、完成家庭作业或完成复杂任务(例如，读书报告、写文章)时很容易

不知所措

- 执行功能障碍，例如，难以记住、安排和完成任务
- 难以理解一般高中课程中的抽象概念，例如，小说中的人物性格发展或动机，以及和平、正义、自由等历史或社会学概念
- 非言语性学习障碍(DSM-5中并未认可该病症)(参见 “儿童特定学习障碍的临床特征”，关于‘非语言型学习困难’一节)

睡眠问题 — ASD患儿可能伴有睡眠问题或障碍，如抗拒就寝、睡眠焦虑、难以入睡、频繁醒来、辗转反侧或睡眠结构异常[87-90]。(参见 “儿童行为睡眠问题”和 “儿童睡眠障碍的评估”)

喂养问题 — 由于ASD患儿有异常感觉行为和感知异常，故可能拒绝或只吃特定味道/口感的食物。这可能引起体重异常、腹泻、便秘等胃肠道症状，或因进食不合理而缺乏营养。(参见上文 ‘异常感觉行为/异常感知’)

躯体疾病或遗传性疾病 — ASD可能与一些躯体疾病(例如，癫痫)、环境因素(例如，丙戊酸胎儿病)或遗传综合征((表 3))相关，详见其他专题。(参见 “孤独症谱系障碍：专业术语、流行病学和发病机制”，关于‘相关疾病和综合征’一节和 “癫痫合并妊娠的相关风险”，关于‘抗癫痫药的远期影响’一节)

其他临床特征

运动缺陷 — ASD患儿可能存在运动缺陷，包括步态异常、笨拙、用脚尖走路或其他异常运动体征，如肌张力过低[29,91]。运动缺陷虽常见[92,93]，但并非ASD的关键特征。(参见 “孤独症谱系障碍的评估和诊断”，关于‘诊断标准’一节)

大头畸形 — 仅患ASD的儿童中，约1/4头围大于第97百分位数[94,95]。多达70%的ASD儿童被发现在出生后第1年期间头部生长速度加快，但这些儿童并非都会变为大头畸形[96-99]。

头部生长加速可能与早期大脑发育过程中的异常有关，这些发育异常导致了ASD的临床表现[96,100]。2-4岁之前，平均脑体积增加，一些患儿出现巨脑症[101,102]。然而，一项具有全国代表性的纵向队列研究纳入了约9000例儿童，结果发现无论是否存在ASD，9个月、24个月及36个月龄儿童的平均头围相近[103]。因此，虽然一些ASD儿童会发生大头畸形，但大头畸形并非诊断的必要条件。

伴大头畸形的ASD患者可能存在PTEN基因突变，这使此类患者存在发生错构瘤综合征的风险[104]。存在大头畸形的ASD患儿中PTEN错构瘤综合征的评估参见其他专题。(参见 “PTEN hamartoma tumor syndromes, including Cowden syndrome”, section on ‘Autism spectrum disorders and macrocephaly’)

特殊技能 — 一些个体虽然在其他领域有严重缺陷，但在记忆、数学、音乐、艺术或拼图等方面有特殊技能(即，“学者”技能)[26,44]。其他特殊技能包括日历计算(测算一个给定日期是星期几)及阅读早慧(自发且过早地掌握单字阅读)[105,106]。这种阅读通常是形式上的，很少理解意思或了解阅读的目的[26]。

学会指南链接

部分国家和地区的学会指南和政府指南的链接参见其他专题。(参见 “Society guideline links: Autism spectrum disorder”)

患者教育

UpToDate提供两种类型的患者教育资料：“基础篇”和“高级篇”。基础篇通俗易懂，相当于5-6年级阅读水平(美国)，可以解答关于某种疾病患者可能想了解的4-5个关键问题；基础篇更适合想了解疾病概况且喜欢阅读简短易读资料的患者。高级篇篇幅较长，内容更深入详尽；相当于10-12年级阅读水平(美国)，适合想深入了解并且能接受一些医学术语的患者。

以下是与此专题相关的患者教育资料。我们建议您以打印或电子邮件的方式给予患者。(您也可以通过检索“患者教育”和关键词找到更多相关专题内容。)

- 基础篇(参见 “患者教育：孤独症谱系障碍(基础篇)”)
- 高级篇(参见 “Patient education: Autism spectrum disorder (Beyond the Basics)”)

总结

- 孤独症谱系障碍(ASD)是一类异质性神经发育障碍，特征为社会交流和社会互动异常以及受限且重复的行为模式，临床表现多种多样。通常在1岁多时发现症状，但也可能更早或到后面其有限的能力无法满足社会需求时才表现出来。(参见上文‘表型谱系和临床表现’)
- 社会交流和互动障碍可能表现为(表 4A-B)：
  - 缺乏社交情感互动，例如，不与他人分享快乐、兴趣和成就，在人际互动中展现或回应兴趣的能力低下
  - 无法在社交中恰当使用注视、面部表情和手势等非言语行为，以及语用交流障碍，例如：在对话中不遵循发言顺序、垄断发言权；难以理解语言含义随情景发生的变化；难以理解幽默和讽刺
  - 难以建立和维持与儿童发育水平相符的同伴关系

(参见上文‘社会交流和互动受损’)

- ASD的行为特征包括：受限且重复的行为、兴趣和活动，例如，刻板重复的运动性作态、顽固遵守非功能性常规或程序；感知异常(表 4A-B)。(参见上文‘受限且重复的行为、兴趣和活动’)
- ASD常伴有智力障碍或语言障碍，还可能与其他遗传、躯体或环境因素有关。做出诊断时应明确指出有无这些相关病症。(参见上文‘伴随病症’)
- 有ASD临床特征的儿童的评估和诊断参见其他专题。(参见 “孤独症谱系障碍的评估和诊断”)

使用UpToDate临床顾问须遵循用户协议.

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专题 627 版本 25.0.zh-Hans.2.0

图表

Early symptoms and signs of autism

Early symptoms and signs of autism
Parental concerns about deficits in social skills
Parental concerns about deficits in language skills or behavior
Parental concerns about frequent tantrums or intolerance to change
Delayed language and social/communication skills: ▪ Lack of orientation to name by age 12 months ▪ Lack of pointing or gesturing to indicate interest (eg, by pointing to an airplane flying over) by age 14 months ▪ Lack of pretend play (eg, "feeding" a doll) by age 18 months
Avoiding eye contact or wanting to be alone
Having trouble understanding other people's feelings or talking about their own feelings
Repeating words or phrases over and over (echolalia)
Giving unrelated answers to questions
Getting upset by minor changes
Having obsessive interests
Flapping their hands, rocking their body, or spinning in circles
Having unusual reactions to the way things sound, smell, taste, look, or feel

Adapted from: Centers for Disease Control and Prevention. Autism spectrum disorder. Signs and symptoms of autism spectrum disorders. Available at: www.cdc.gov/ncbddd/autism/signs.html (Accessed on January 02, 2020).

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Differential diagnosis of autism spectrum disorder

Condition	Features that may help distinguish the condition from ASD
Global developmental delay/intellectual disability	▪ Social responsiveness and communication appropriate for developmental level
Intellectual giftedness	▪ Normal pragmatic language skills ▪ Intense interests are functional, varied, and can be explained by the child ▪ Social interaction is generally enjoyed
Social (pragmatic) communication disorder	▪ Absence of restricted, repetitive patterns of behavior, interests, or activities
Developmental language disorder	▪ Normal reciprocal social interactions ▪ Normal desire and intent to communicate ▪ Appropriate imaginative play
Language-based learning disorder	▪ Normal reciprocal social interactions ▪ Normal desire and intent to communicate ▪ Appropriate imaginative play ▪ Pragmatic language more typical than in ASD ▪ Desire to communicate (even if competency is lacking)
Nonverbal learning disorder	▪ Impairment in social skills and pragmatic language milder than in ASD ▪ Lack of restricted, repetitive patterns of behavior, interests, or activities
Hearing impairment	▪ Normal reciprocal social interactions ▪ Normal eye-to-eye gaze ▪ Facial expressions indicate intention to communicate
Landau-Kleffner syndrome	▪ Usually have typical development until approximately 3 to 6 years of age ▪ Typically presents with auditory verbal agnosia (behaving as if deaf)
Rett syndrome	▪ Female predominance ▪ Head growth deceleration ▪ Stereotypic hand movements ▪ Gait abnormalities ▪ Abnormal respiratory pattern
Fetal alcohol spectrum disorder	▪ Characteristic facial features (not always present): • Short palpebral fissures • Thin vermillion border • Smooth philtrum
Attachment disorder	▪ History of severe neglect or mental health issues in caregiver ▪ Social deficits tend to improve in appropriate caregiving environment
Attention deficit hyperactivity disorder	▪ Normal pragmatic language skills ▪ Normal nonverbal social behavior ▪ Normal imaginative play ▪ Lack of restricted, repetitive patterns of behavior, interests, and activities
Anxiety disorder (includes social anxiety and selective mutism)	▪ Normal nonverbal social behavior and imaginary play ▪ Lack of circumscribed interests ▪ Absence of restricted, repetitive patterns of behavior, interests, or activities
Obsessive compulsive disorder	▪ Normal social skills ▪ Normal pragmatic language ▪ Symptoms are a source of anxiety rather than a pleasure

Stereotypic movement disorder	▪ Normal social skills ▪ Normal pragmatic language
Tic disorder/Tourette syndrome	▪ Normal social skills ▪ Normal pragmatic language

The differential diagnosis of ASD includes a number of conditions that impair social communication or social interaction and/or are associated with stereotypic movements. In some cases, these conditions are the cause of the ASD-like symptoms and the child does not have ASD; in other cases, the conditions co-occur with ASD. Refer to UpToDate content on evaluation of ASD in children for additional details.

ASD: autism spectrum disorder.

Graphic 119225 Version 3.0

Selected genetic syndromes associated with autism spectrum disorder

Syndrome	Clinical features
Tuberous sclerosis complex (TSC) (TSC1 and TSC2)	▪ Hypopigmented macules ▪ Angiofibromas ▪ Shagreen patches ▪ Benign tumors in multiple organs ▪ Seizures ▪ Cognitive deficits
Fragile X syndrome	▪ Long, narrow face ▪ Prominent forehead and chin ▪ Large ears ▪ Testicular enlargement in adolescence ▪ Macrocephaly ▪ Arched palate ▪ Hyperextensible joints
Chromosome 15q11-q13 duplication syndrome	▪ Hypotonia ▪ Joint laxity ▪ Global developmental delays, particularly motor delays ▪ Seizures ▪ Speech delay ▪ Social deficits ▪ Stereotypies ▪ Variable pattern of mild facial dysmorphism
Angelman syndrome	▪ Severe intellectual disability ▪ Postnatal microcephaly ▪ Movement/balance problems ▪ Language delay ▪ Seizures
Rett syndrome	▪ Occurs almost exclusively in females ▪ Loss of speech ▪ Replacement of purposeful with stereotypic hand movements ▪ Gait abnormalities ▪ Abnormal respiratory pattern
Cohen syndrome	▪ Thick hair and eyebrows ▪ Wave-shaped palpebral fissures ▪ Broad nasal tip ▪ Short or smooth philtrum ▪ Microcephaly ▪ Poor weight gain in infancy ▪ Truncal obesity in adolescence ▪ Hypotonia ▪ Developmental delay ▪ Neutropenia ▪ Joint hypermobility
Cornelia de Lange syndrome (CDLS) CDLS1, CDLS2, CDLS3, CDLS4, CDLS5	▪ Microcephaly ▪ Synophrys ▪ Highly-arched eyebrows ▪ Anteverted nares ▪ Prenatal onset growth delay

	▪ Hirsutism ▪ Upper-limb reduction deficits ▪ Hearing impairment ▪ Myopia ▪ Cardiac septal defects ▪ Gastrointestinal dysfunction ▪ Genitourinary abnormalities
Neurofibromatosis type 1	▪ Multiple café-au-lait macules ▪ Axillary and/or inguinal freckling ▪ Lisch nodules (iris hamartomas) ▪ Neurofibromas
Down syndrome	▪ Upslanting palpebral fissures ▪ Epicanthic folds ▪ Brachycephaly ▪ Transverse palmar crease ▪ Intellectual disability ▪ Medical conditions (eg, cardiovascular disease, gastrointestinal abnormalities, endocrine disorders)
Noonan syndrome (multiple types)	▪ Short stature ▪ Congenital heart disease (most often pulmonic stenosis) ▪ Delayed development
Williams-Beuren syndrome	▪ "Elfin" facies ▪ Systemic arterial stenosis (most often supravalvular aortic stenosis) ▪ Short stature ▪ Genitourinary abnormalities ▪ Impaired cognition and development
DiGeorge (22q11.2 deletion) syndrome	▪ Conotruncal cardiac anomalies ▪ Hypoplastic thymus ▪ Hypocalcemia
PTEN-associated macrocephaly syndromes	
▪ Macrocephaly/autism syndrome	▪ Postnatal macrocephaly ▪ Broad forehead ▪ Frontal bossing ▪ Long philtrum ▪ Depressed nasal bridge ▪ Intellectual disability
▪ Cowden/Bannayan-Riley-Ruvalcaba syndrome	▪ Macrocephaly ▪ Birdlike facies ▪ Hypoplastic mandible and maxilla ▪ Cataract ▪ Microstomia ▪ High-arched palate ▪ Pectus excavatum ▪ Genitourinary anomalies ▪ Skin tags ▪ Lipomas ▪ Penile macules
CHARGE syndrome	▪ **C**oloboma of the eye ▪ **H**eart defects ▪ Choanal **a**tresia

	▪ Growth **r**etardation ▪ **G**enitourinary anomalies ▪ **E**ar abnormalities
Joubert syndrome	▪ Hypoplasia of the cerebellar vermis ▪ Neurologic symptoms ▪ Retinal dystrophy ▪ Renal anomalies
Smith-Lemli-Opitz syndrome	▪ Postnatal microcephaly ▪ Soft cleft palate/bifid uvula ▪ Micrognathia ▪ Low-set posteriorly rotated ears ▪ Poor weight gain ▪ Syndactyly of the second and third toes ▪ Abnormal genitalia ▪ Intellectual disability ▪ Hypotonia
Timothy syndrome	▪ Syndactyly ▪ Congenital heart disease ▪ Multiorgan dysfunction ▪ Cognitive abnormalities

PTEN: phosphate and tensin homolog gene.

Graphic 117770 Version 5.0

Possible symptoms of autism spectrum disorder in preschool-age children[1-4]

Impairments in social communication and interaction
▪ Lack of, delay, or regression in spoken language.
▪ If present, spoken language may be atypical, for example: • Unusual intonations (monotone, sing-song) • Echolalia • Incorrect pronoun use (referring to self by name or as "you," "he," or "she" after age 3 years) • Non-speech-like vocalizations (eg, grunting, squealing) • Limited to specific topics of interest
▪ Limited use of language for communication (eg, using only single words even though capable of speaking in sentences).
▪ Reduced or absent nonverbal communication (gestures, facial expression).
▪ Little or no response to others' gestures or facial expression.
▪ Lack of response or slow to respond when called by name (despite normal hearing).
▪ Reduced or absent interest in or attempts to share interest with another person (eg, by pointing or monitoring the other's gaze), for example: • Lack of social smile or eye contact • Lack of imitation (eg, clapping) • Limited or absent social bids • Lack of ability of interest in sustaining a social interaction • Resistance to being be cuddled
▪ Lack of awareness of other people; appearing to be in their own world.
▪ Preference for solitary play (lack of initiation or participation in social play with others).
▪ Lack of interest in other children or odd social approaches to other children (eg, disruptive, aggressive).
▪ Lack of awareness of common social conventions (eg, taking turns in a conversation, awareness of personal space).
▪ Lack of or minimal recognition or responsiveness to another's feelings (eg, happiness, distress).
▪ Abnormal interactions with peers or adults (eg, too friendly or too distant).
▪ Normal or even exaggerated level of motivation to socialize, with limited ability to infer the intentions or behaviors of others.
▪ Motivated to socialize but not able to sustain a social interaction that is mutually enjoyable due to not respecting social conventions, due to an inability to anticipate the knowledge and interests of others, etc. For example, does not respect personal boundaries; may talk only about preferred interests and not engage in the social partner's interests.
Restricted, repetitive behaviors, interests, and activities
▪ Repetitive motor mannerisms (eg, hand flapping).
▪ Resistance to change, insistence on following same routines.
▪ Re-enacting scenes from videos or cartoons.
▪ Atypical play: • Repetitive (eg, lines up objects, opens and closes doors, turns lights on and off) • Lacking imaginative/creative play • No pretend play (eg, feeding doll) • Over-attention to parts of objects (eg, spinning wheels)

- Lack of or unusual reaction to sensory stimuli (noise, texture, smells).

This table is intended for use in conjunction with UpToDate content on ASD. The list of symptoms is not all inclusive. It is meant to prompt clinicians to consider the possibility of ASD. Additional criteria and comprehensive evaluation are necessary for diagnosis. Refer to UpToDate content on ASD for details.

ASD: autism spectrum disorder.

References:

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Possible symptoms of autism spectrum disorder in school-age children and adolescents[1-4]

Impairments in social communication and interaction
▪ Abnormal language development, including muteness
▪ If present, spoken language may be atypical; for example: • Unusual prosody of speech (rate, rhythm, tone, volume) • Persistent echolalia • Referring to self by name or as "you," "he," or "she" • Non-speech-like vocalizations • Tendency to speak freely only about specific topics of interest • Talking at others rather than having a back-and-forth conversation • Unusual vocabulary for age or social group • Responses to others may seem rude or inappropriate • Difficulty understanding others' intentions (eg, takes things literally, misunderstands metaphors or sarcasm) • Unable to adapt style of communication to social situations (eg, overly formal or inappropriately familiar) • Reduced and poorly integrated gestures, facial expressions, body orientation, and eye contact
▪ Limited use of language for communication
▪ Reduced, absent, or atypical nonverbal communication (eye contact, gestures, facial expression)
▪ Poor response to name (despite normal hearing)
▪ Little or no response to others' gestures or facial expressions
▪ Reduced interest in people, including children their own age
▪ Apparent preference for aloneness
▪ Difficulty making and maintaining peer friendships (may find it to be easier with younger children or adults)
▪ Reduced or lack of enjoyment of situations that most other children enjoy (eg, birthday parties)
▪ Difficulty joining in play of other children (eg, makes no effort to join in or uses wrong approach [eg, aggressive, disruptive])
▪ Difficulty interacting in unstructured social situations (eg, school recess)
▪ Poor understanding or following of social conventions (eg, greetings, farewell behaviors, taking turns, classroom behavior, awareness of personal space)
▪ Easily overwhelmed by social or other types of stimulation, for example: • Extreme reactions to invasion of personal space • Resistance to being hurried
▪ Reduced or absent response to others' feelings
▪ Extremes of emotional reactivity that are excessive for circumstances
▪ Abnormal interactions with adults (no interaction or too intense)
Restricted, repetitive behaviors, interests, and activities
▪ Lack of flexible, cooperative, imaginative play or creativity, for example: • Rigid expectation that other children adhere to rules of play • Strong adherence to rules of fairness (may lead to arguments) • Repeatedly reenacting scenes from videos or cartoons • Preference for highly specific, narrow interests or hobbies (eg, collecting, listing, numbering)

• Difficulty with imagination (eg, in writing, for future planning)
▪ Preoccupation with restricted patterns of interest that are abnormal in intensity or focus and interfere with activities of daily life
▪ Strong preference for familiar routines
▪ Inability to cope with change or situations that lack structure (may lead to distress [eg, anxiety, aggression])
▪ Aberrant response to sensory stimuli (over- or under-sensitive), for example: • Excessively touching people or objects • Preferring to be in the dark • Deliberately smelling objects

This table is intended for use in conjunction with UpToDate content on ASD. The list of symptoms is not all inclusive. It is meant to prompt clinicians to consider the possibility of ASD. Additional criteria and comprehensive evaluation are necessary for diagnosis. Refer to UpToDate content on ASD for details.

ASD: autism spectrum disorder.

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1. *Hyman SL, Levy SE, Myers SM, Council on Children with Disabilities, Section on Developmental and Behavioral Pediatrics. Identification, evaluation, and management of children with autism spectrum disorder. Pediatrics 2020; 145.*
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Graphic 119808 Version 4.0

Contributor Disclosures

Marilyn Augustyn, MD No relevant financial relationship(s) with ineligible companies to disclose. **L Erik von Hahn, MD** Other Financial Interest: Brookes Publishing royalties [Childhood education]. All of the relevant financial relationships listed have been mitigated. **Marc C Patterson, MD, FRACP** Equity Ownership/Stock Options: IntraBio [General lysosomal diseases and ataxic disorders]. Grant/Research /Clinical Trial Support: Orphazyme [Niemann-Pick disease, type C]; Shire [Metachromatic leukodystrophy]; Amicus [Late-onset Pompe disease]; Glycomine [Congenital disorders of glycosylation]. Consultant/Advisory Boards: Actelion [Niemann-Pick C]; Amicus [Fabry disease, Gaucher disease, Pompe disease]; Cerecor [Congenital disorders of glycosylation]; IntraBio [General lysosomal diseases and ataxic disorders]; Novartis [Multiple sclerosis]; Orphazyme [Niemann-Pick disease, type C]; Shire [Metachromatic leukodystrophy]. Other Financial Interest: Sage [Child neurology]; Wiley [JIMD]. All of the relevant financial relationships listed have been mitigated. **Mary M Torchia, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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