



AIDA
Autism Infectious Disease Alliance

CLINICAL GUIDE NO. 001

Medical Evaluation Guide for Children with Autism

Recognizing Multisystem Illness to Improve Comprehensive Patient Care

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About This Guide

The Autism Infectious Disease Alliance (AIDA) developed this clinical guide to encourage a proactive, comprehensive medical evaluation of autistic children for medical conditions commonly associated with autism. Many autistic children experience symptoms involving the immune system, nervous system, gastrointestinal tract, autonomic nervous system, connective tissue, endocrine system, and other organ systems. Early recognition of these conditions may support more timely intervention, improve quality of life, and help optimize overall medical care.

Autism is diagnosed behaviorally, yet many autistic children experience complex medical symptoms that extend well beyond the diagnostic criteria. Whether these medical conditions contribute to autism, result from shared underlying biological processes, or develop alongside autism continues to be investigated. Regardless of the underlying mechanism, recognizing and appropriately evaluating these medical conditions is an important component of comprehensive patient care.

The purpose of this guide is to assist healthcare professionals in recognizing medical signs and symptoms that may warrant further evaluation. It provides a practical framework for obtaining a comprehensive history, performing a targeted physical examination, considering appropriate laboratory testing, and making referrals based on each child's individual clinical presentation.

For many families, medical concerns may be attributed to autism itself rather than evaluated as medical conditions commonly associated with autism that may warrant further investigation. A broader medical assessment may help identify health conditions that contribute to physical discomfort, behavioral changes, anxiety, sleep disturbance, gastrointestinal symptoms, pain, or other challenges affecting daily life. This is particularly important for children who are non-speaking, minimally speaking, very young, or otherwise unable to fully communicate their symptoms or advocate for themselves.

This guide is intended to support earlier recognition of medical conditions commonly associated with autism and to encourage comprehensive, multidisciplinary care. It does not establish standards of care, recommend specific treatments, or replace clinical judgment. Diagnostic testing, referrals, and management decisions should always be individualized based on each patient's history, physical examination, and clinical presentation.

Additional educational resources, references, and updates are available through the Autism Infectious Disease Alliance. Readers seeking a more comprehensive review of the scientific literature, the prevalence of these commonly associated medical conditions, shared neuroinflammatory findings, and the evidence supporting the concepts presented in this guide may also refer to *A Blind Spot on Autism: Rethinking What Could Be Driving the Autism Pandemic* by Debbie Kimberg and Edward B. Breitschwerdt, DVM.

Introduction

CDC surveillance data from 2022 identified autism spectrum disorder in approximately one in every thirty-one 8-year-old children across 16 monitoring sites in the United States. Although autism is diagnosed based on behavioral criteria, many autistic individuals experience a broad range of medical symptoms involving the immune system, nervous system, gastrointestinal tract, connective tissue, autonomic nervous system, endocrine system, and other organ systems.

A growing body of research has documented the high prevalence of these medical conditions in autistic individuals. These conditions may contribute to symptom severity, functional impairment, behavioral changes, quality of life, and overall health. Yet many autistic children continue to receive predominantly behavioral evaluations while potentially significant medical findings remain underrecognized or untreated.

A comprehensive medical assessment does not challenge an autism diagnosis. Rather, it complements the diagnostic evaluation by helping identify medical conditions commonly associated with autism that may warrant further investigation, treatment, or referral. Early recognition of these conditions may improve health outcomes, reduce suffering, and enhance quality of life.

This guide encourages clinicians to look beyond behavior alone by incorporating a comprehensive medical history, review of systems, family history, environmental exposures, physical examination, and targeted laboratory evaluation when clinically appropriate. Its goal is to support earlier recognition of medical conditions associated with autism and promote comprehensive, patient-centered care.

Purpose of This Guide

This guide was developed to assist healthcare professionals in providing a comprehensive medical evaluation for autistic children. Its goal is to promote proactive identification of medical conditions commonly associated with autism through routine history taking, physical examination, and appropriate diagnostic evaluation.

Its objectives are to:

- Encourage recognition of autism as a condition that commonly involves multiple organ systems.
- Promote a comprehensive medical evaluation that extends beyond the behavioral features of autism.
- Support routine review of systems and family history to identify medical conditions that may otherwise go unrecognized.
- Highlight clinical findings that may warrant additional diagnostic evaluation.
- Support thoughtful use of laboratory testing based on each patient's history, symptoms, and physical examination.
- Encourage timely treatment or referral when indicated.
- Foster collaboration among healthcare professionals involved in the care of autistic individuals.

Ultimately, this guide is intended to support comprehensive, proactive, and individualized medical care for autistic children. By encouraging earlier recognition and evaluation of medical conditions commonly associated with autism, clinicians may help improve health, reduce unnecessary suffering, and enhance quality of life.

Autism as a Multisystem Medical Condition

DRAFTING PLACEHOLDER

Insert the Chapter 4 prevalence table as the centerpiece of this section. The final table should use the exact prevalence ranges and source citations from A Blind Spot on Autism.

Mast Cell Activation Syndrome (MCAS)

DRAFTING PLACEHOLDER

Draft a concise, one-page explanation of MCAS followed by the approved multisystem symptom table. Include only symptoms and claims supported by the book and its references.

Looking Beyond Behavior

DRAFTING PLACEHOLDER

Insert the behavior-to-possible-medical-causes table. The table should help clinicians investigate pain, gastrointestinal symptoms, infection, inflammation, sleep problems, anxiety, intrusive thoughts, autonomic symptoms, and other potential contributors before attributing a change solely to autism.

Communication Matters

Communication is a fundamental human right. Every autistic child deserves the opportunity to communicate pain, discomfort, emotions, preferences, and medical symptoms, regardless of their verbal abilities.

Clinicians should avoid making assumptions about a child's cognitive abilities based solely on limited speech, lack of eye contact, motor differences, repetitive movements, or other atypical behaviors. Many autistic individuals understand considerably more than they are able to express.

The inability to communicate can contribute to profound stress, frustration, anxiety, social isolation, and delayed recognition of underlying medical conditions. Supporting effective communication is therefore an essential component of comprehensive medical care.

Whenever possible, clinicians should encourage families to explore communication methods that best match their child's strengths and needs so that the child can participate meaningfully in their own healthcare and communicate symptoms as their abilities develop.

Comprehensive Multisystem Review of Symptoms

DRAFTING PLACEHOLDER

Complete the rapid symptom checklist under the approved categories below. The finished tool should take only a few minutes to review and should lead directly to focused examination and testing rather than becoming a lengthy intake instrument.

- Neuropsychiatric and Cognitive
- Neurologic
- Sleep
- Autonomic
- Gastrointestinal and Feeding
- Musculoskeletal, Connective Tissue, and Pain
- Dermatologic
- Immune and Infectious
- Cardiovascular and Respiratory
- Genitourinary

Practical Considerations

General questions such as “Is everything okay?” often fail to uncover symptoms in autistic children. Clinicians should ask specific questions about eating, sleep, bowel habits, pain, dizziness, skin changes, activity level, and

behavior. Caregivers should also be asked whether new behaviors may represent an attempt to communicate discomfort, pain, or illness.

Comprehensive Family History

DRAFTING PLACEHOLDER

Complete the family history checklist. Every subsection will begin with “Why ask?” followed by a concise checklist. Add long COVID to the family history content.

- Autoimmune disease
- Neurodevelopmental and neuropsychiatric disorders
- Connective tissue and autonomic disorders
- Allergic and inflammatory conditions
- Pregnancy and maternal history
- Environmental and animal exposures

Practical Considerations

Family history extends beyond genetics. Patterns of illness, shared environmental exposures, infectious exposures, immune-mediated disorders, and chronic inflammatory conditions may provide valuable clinical clues. Even when a family member has never received a formal diagnosis, recurring symptom patterns can help guide a more comprehensive medical evaluation.

Comprehensive Physical Examination

DRAFTING PLACEHOLDER

Complete the focused physical examination checklist under the approved categories below. The skin examination should include Bartonella-associated lesions, described as reddish, bluish, or blanched, with a QR code linking to the approved educational resource.

- General examination
- Skin examination
- Lymphatic examination
- Musculoskeletal and connective tissue examination
- Neurologic examination
- Autonomic evaluation
- Oral examination

Practical Considerations

Many examination findings are subtle and should be interpreted within the context of the child’s history, review of systems, and overall clinical presentation. While no individual finding is diagnostic, identifying multiple abnormalities across different organ systems may support a more comprehensive diagnostic evaluation.

Comprehensive Diagnostic Screening

The goal of diagnostic screening is to identify medical conditions that may contribute to an autistic child's overall clinical presentation. Laboratory testing should always be guided by the child's history, comprehensive review of symptoms, family history, physical examination, and clinical judgment. No single laboratory test can diagnose autism or explain every symptom. Rather, testing should be used to identify potentially treatable medical conditions and guide further evaluation.

Many autistic children present with symptoms affecting multiple organ systems. Whenever possible, clinicians should seek a coordinated diagnostic approach that looks for underlying disease processes capable of explaining the child's complete clinical picture before pursuing fragmented evaluations focused on individual symptoms.

General Health Screening

Why screen?

Baseline laboratory testing may identify nutritional deficiencies, endocrine disorders, systemic inflammation, hematologic abnormalities, or other common medical conditions that may contribute to fatigue, behavioral changes, poor growth, chronic illness, or neuropsychiatric symptoms.

Consider:

- Complete Blood Count (CBC) with Differential
- Comprehensive Metabolic Panel (CMP)
- C-Reactive Protein (CRP)
- Erythrocyte Sedimentation Rate (ESR)
- Ferritin
- Vitamin B12
- Vitamin D (25-hydroxy)
- Serum Copper
- Ceruloplasmin
- Thyroid Panel: TSH, Free T4, and Free T3
- Celiac Panel: Tissue Transglutaminase IgA (tTG-IgA) and Total IgA
- Urinalysis

Immune Function Evaluation

Why screen?

Immune abnormalities have been reported in many autistic individuals and may contribute to recurrent infections, chronic inflammatory symptoms, neuropsychiatric symptoms, fatigue, or poor recovery from illness.

Consider:

- Quantitative Immunoglobulins: IgG, IgA, IgM, and IgE
- IgG Subclasses (1–4)
- Streptococcus pneumoniae Serotype Antibodies
- Antinuclear Antibody (ANA)
- Glutamic Acid Decarboxylase (GAD-65) Antibodies

Neuroinflammatory Evaluation

Why screen?

Neuroinflammatory biomarkers may provide evidence of immune activation in children with persistent neuropsychiatric symptoms, behavioral regression, chronic fatigue, chronic pain, multisystem illness, or other findings suggestive of neuroinflammation. These markers are nonspecific and should always be interpreted within the context of the child's complete clinical presentation.

Consider:

- Cytokine Panel
- Interleukin-6 (IL-6)
- Tumor Necrosis Factor-alpha (TNF-α)
- Interleukin-1 beta (IL-1β)
- Interleukin-12 (IL-12)
- Interferon-gamma (IFN-γ)
- Monocyte Chemoattractant Protein-1 (MCP-1)
- Vascular Endothelial Growth Factor (VEGF)

PANS-Related Evaluation

Why screen?

Children with obsessive compulsive symptoms, restrictive eating, emotional lability, tics, behavioral regression, or other symptoms consistent with PANS should be evaluated for potential infectious or inflammatory triggers, regardless if there were acute-onset of symptoms.

Consider:

- Rapid Group A Streptococcus Test
- Throat Culture
- Perianal or Vaginal Streptococcal Culture
- Antistreptolysin O (ASO) Titer
- Anti-DNase B Titer
- Streptozyme Test

Mast Cell Activation Syndrome

DRAFTING PLACEHOLDER

Insert the MCAS laboratory evaluation from the book after clinical and scientific review. Testing should be matched to symptoms, specimen handling requirements, and the child's complete clinical presentation.

Infectious Disease Evaluation

Why screen?

Children with multisystem symptoms, neuropsychiatric changes, chronic inflammatory symptoms, compatible environmental exposures, suggestive physical findings, or a family history raising concern for infectious disease may warrant further evaluation.

Bacterial Pathogens

- Bartonella species
- Borrelia burgdorferi (Lyme disease)
- Mycoplasma pneumoniae

Protozoan Parasites

- Babesia species

Viral Evaluation

- Epstein-Barr Virus (EBV)
- Human Herpesvirus-6 (HHV-6)
- Herpes Simplex Virus (HSV-1 and HSV-2)
- Cytomegalovirus (CMV)
- Coxsackie A and B
- Influenza A and B, when clinically indicated
- COVID-19 testing, when clinically indicated

Testing note

Commercial laboratory testing may have limitations for some vector-borne infections. The final guide will provide carefully reviewed language explaining when complementary or specialty testing may be appropriate. Laboratories discussed in *A Blind Spot on Autism* include Galaxy Diagnostics, IGeneX, T-Lab, Vibrant America, and ArminLabs in Europe.

Environmental Evaluation

DRAFTING PLACEHOLDER

Complete the environmental evaluation using only markers and testing discussed in A Blind Spot on Autism.

Practical Considerations

Diagnostic screening should complement, not replace, a careful history and physical examination. Laboratory abnormalities are rarely diagnostic in isolation, and normal results do not exclude disease. Results should always be interpreted within the context of the child's complete clinical presentation.

Whenever possible, clinicians should seek the fewest number of medical conditions that best explain the child's multisystem symptoms. A coordinated diagnostic approach may reduce unnecessary testing, minimize fragmented care, and improve identification of potentially treatable medical conditions.

When Findings Suggest Possible Infection-Associated Chronic Illness

Why Evaluate?

Infection-associated chronic illness, or IACI, is an umbrella term used to describe chronic illnesses, introduced by HHS in 2026, that develop following an infection, including stealth unrecognized infections, and may involve overlapping symptoms such as fatigue, pain, cognitive difficulties, autonomic dysfunction, immune dysregulation, and neuroinflammation.

Autism is not currently classified as an IACI. However, some autistic children present with developmental, neuropsychiatric, inflammatory, autonomic, gastrointestinal, dermatologic, musculoskeletal, and other medical symptoms that may warrant evaluation for an underlying infectious or immune-mediated process.

In young children, including those with possible congenital exposure, symptoms of infection may be difficult to recognize. Pain, fatigue, nausea, dizziness, intrusive thoughts, sensory changes, and other internal symptoms may instead appear as irritability, withdrawal, sleep disturbance, restrictive eating, regression, aggression, self-injury, or other behavioral changes. These symptoms should not automatically be attributed to autism.

Recognizing a Clinical Pattern

No single symptom, examination finding, or laboratory result establishes that an infection is contributing to a child's clinical presentation. Concern should increase when several findings occur together, particularly when multiple organ systems are involved.

Clinical patterns that may warrant further investigation include:

- Developmental, behavioral, or functional regression.
- Development, sometimes abruptly, of changes in mood, anxiety, obsessive compulsive symptoms, tics, restrictive eating, emotional regulation, or sleep.
- Unexplained pain involving the joints, muscles, bones, nerves, abdomen, head, or soles of the feet.
- Persistent fatigue, reduced stamina, exercise intolerance, weakness, or prolonged recovery following activity or illness.
- Dizziness, faintness, temperature dysregulation, unusual sweating, palpitations, low blood pressure, air hunger, or other autonomic symptoms.
- Gastrointestinal symptoms combined with neurologic, behavioral, immune, or inflammatory findings.
- Recurrent infections, prolonged illness, poor recovery from infection, or evidence of immune dysfunction.
- Unusual dermatologic findings, including reddish, bluish, or blanched linear skin lesions that resemble stretch marks but do not follow the lines of the skin.
- Lymph node enlargement, unexplained fevers, chills, sweats, pallor, jaundice, or hematologic abnormalities.
- Symptoms that fluctuate, relapse, migrate, or worsen following an infection, physical stress, or immune challenge.
- Findings involving several organ systems without another diagnosis that adequately explains the complete clinical presentation.

Neuroinflammatory and PANS-Related Clues

Neuroinflammatory biomarkers and findings associated with PANS are nonspecific and cannot identify the cause of a child's symptoms independently. However, when these findings occur alongside a compatible clinical presentation, they may provide clues that an infectious or inflammatory contributor warrants further evaluation.

Relevant findings may include:

- Abnormal inflammatory markers.
- Abnormal cytokines or other neuroinflammatory markers.
- Evidence of immune activation, immune deficiency, or autoimmunity.
- Abrupt onset or worsening of obsessive compulsive symptoms, restrictive eating, tics, emotional lability, anxiety, urinary symptoms, sleep disturbance, regression, or deterioration in school performance.
- Neurologic abnormalities, cognitive changes, motor changes, sensory changes, or altered pain perception.
- Mast cell, autonomic, connective tissue, gastrointestinal, or other multisystem abnormalities occurring with neuropsychiatric symptoms.

Laboratory findings should be interpreted within the context of the child's history, family history, exposures, physical examination, and complete clinical presentation.

Family, Maternal, and Exposure History

The possibility of an infection-associated illness should not be evaluated solely through a history of a known tick bite. Many children and families do not recall a bite, and some infections can be transmitted through other routes.

Relevant clinical clues may include:

- Similar multisystem symptoms in a parent, sibling, or other close relative.
- Maternal illness before or during pregnancy.
- Possible congenital or perinatal infection.
- Pregnancy complications, placental abnormalities, premature delivery, or unexplained pregnancy loss.
- Family history of PANS, autoimmune disease, immune deficiency, mast cell activation syndrome, dysautonomia, connective tissue disorders, long COVID, Lyme disease, or chronic unexplained illness.
- Exposure to ticks, fleas, lice, biting flies, mosquitoes, mites, or other arthropods.
- Contact with cats, dogs, wildlife, farm animals, animal scratches, or animal bites.
- Geographic, occupational, household, or travel exposures relevant to infectious disease.

Family clustering does not establish congenital or household transmission. However, similar symptoms among biologically related or closely exposed family members may provide clinically relevant information and help guide further investigation.

Pathogen-Directed Evaluation

Bartonella Species

Evaluation may be appropriate when the child has a compatible combination of neuropsychiatric symptoms, neurologic findings, pain, fatigue, lymph node abnormalities, ocular symptoms, unusual skin lesions, or otherwise unexplained multisystem illness.

Babesia Species

Evaluation may be appropriate when symptoms include unexplained fatigue, sweats, chills, pallor, jaundice, air hunger, exercise intolerance, autonomic symptoms, sleep disturbance, or hematologic abnormalities. Babesia species are protozoan parasites and should not be classified as bacterial pathogens.

Borrelia Species

Evaluation for Lyme disease or another Borrelia infection may be appropriate when the child has compatible exposure, migratory musculoskeletal pain, arthritis, facial palsy, neurologic symptoms, cardiac findings, or possible tick-borne coinfection.

Streptococcal and Other Infectious Triggers

Children with acute onset or significant worsening of obsessive compulsive symptoms, restrictive eating, tics, regression, emotional lability, or other findings consistent with PANS should receive a comprehensive evaluation for potential infectious and inflammatory triggers. Testing for streptococcal infection and other pathogens should be directed by the child's clinical presentation and exposure history.

Other bacterial, viral, fungal, or parasitic infections may warrant evaluation when supported by the child's history, physical examination, immune status, and clinical findings.

Selecting and Interpreting Testing

Different tests provide different types of information. Antibody testing may reflect previous exposure and does not necessarily establish active infection. Direct detection methods may provide stronger evidence of current infection, but sensitivity can vary by pathogen, specimen type, disease stage, organism burden, testing method, and prior treatment.

When selecting testing, clinicians should consider:

- Whether the test detects antibodies, antigens, DNA, RNA, organisms, or a host immune response.
- Whether the specimen and collection timing are appropriate for the suspected pathogen.
- Whether the child's immune status could affect antibody production.
- Whether previous antimicrobial or immune-modulating treatment could affect results.
- Whether repeat or complementary testing may be clinically appropriate.
- Whether evaluation for more than one infection is warranted based on the presentation and exposure history.

Positive results should be interpreted according to the test's validated clinical meaning. Negative results should be considered alongside the sensitivity and limitations of the specific test used. Neither positive nor negative findings should be interpreted in isolation.

When to Refer

Referral to an appropriately experienced clinician may be warranted when the child has:

- Persistent multisystem symptoms without an adequate explanation.
- Developmental, behavioral, cognitive, or functional regression.
- Significant neuropsychiatric changes accompanied by inflammatory, immune, neurologic, autonomic, dermatologic, gastrointestinal, or pain symptoms.
- Findings consistent with PANS or another neuroimmune condition.
- Abnormal immune or neuroinflammatory findings.
- Possible congenital exposure or similar illness among family members.
- Strong clinical concern for infectious disease despite inconclusive initial testing.
- A need for specialized infectious disease, immunology, neurology, rheumatology, gastroenterology, hematology, cardiology, autonomic, or mast cell evaluation.

Practical Considerations

Evaluation for infection-associated chronic illness should be individualized and should not be based on a single symptom, biomarker, or exposure. Autism alone is not an indication for indiscriminate infectious disease testing. Further evaluation is most appropriate when the child has a compatible clinical presentation supported by the history, multisystem symptom pattern, physical examination, laboratory findings, or relevant exposures.

When several abnormalities occur across different organ systems, clinicians should consider whether one or more underlying medical processes could explain the child's complete presentation. A coordinated evaluation may help reduce fragmented care, identify treatable medical conditions, and improve the child's health, comfort, function, and quality of life.

Sections Remaining

DRAFTING PLACEHOLDER

The following sections remain to be developed after the clinical content above is reviewed and finalized.

- Diagnostic Strategy
- Clinical Decision Algorithm
- Referral Directory or Referral Considerations
- References
- QR Codes
- About the Autism Infectious Disease Alliance

Working Draft Notes

Scope

This working draft combines the prose and approved outlines developed to date. Gray drafting boxes identify sections that have not yet been written. Laboratory recommendations and pathogen-specific statements require final clinical and reference review before publication.

Intended format

The final guide is intended to be a concise, action-oriented physician reference. A clinician should be able to scan the symptom, history, examination, and laboratory sections within a few minutes and identify appropriate next steps.