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Autism Screening or Smoke Screen and Mirrors?

Craig M. Powell, MD, PhD

Department of Neurology & Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas; Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas

Parents are constantly “screening” their children from birth, anxiously making sick-visit appointments with their pediatrician for issues as simple as transient neonatal acne, “stork bite” nevus complex, or an occasional viral illness. Parents excitedly watch for developmental milestones—eg, eye contact, cooing, social smile, babbling, sitting, crawling. In every state of the union, early childhood intervention programs are mandated to formally evaluate and in many cases treat every child whose parents have a developmental concern prior to age 3 years. Developmental assessments are performed by a clinical care professional at each pediatrician visit. If parents raise a developmental concern, they are reassured and the child is further tested or referred to specialists or early childhood intervention. In addition, the American Academy of Pediatrics recommends universal screening for autism spectrum disorder (ASD) at ages 18 and 24 months, while the American Academy of Neurology and the Child Neurology Society recommend developmental surveillance at all well-child visits at least through school age. The US Preventive Services Task Force (USPSTF) has commissioned an evidence-based review of screening for ASD in young children. This detailed, thorough monograph is now published in *JAMA*.¹ The report concludes, deceptively simply but accurately, that more research is needed to determine the benefits and harms of screening the general population. A USPSTF draft recommendation statement available online summarizes: “There is not enough evidence available now on the potential benefits and harms of ASD screening in young children to recommend for or against this screening.”² As scientists and physicians, it is important for us to recognize that this is not a recommendation at all but rather a “call to arms” in the struggle to help patients and families affected by ASD find their way to optimal outcomes.

Autism spectrum disorder screening works to identify children with ASD and with other non-ASD diagnoses or developmental concerns.¹ Screening with the Modified Checklist for Autism in Toddlers With Follow-Up Interview (M-CHAT/F) or the revised version of M-CHAT/F (M-CHAT R/F) has a positive predictive value for ASD of about 50%. While this may sound like the toss of a coin, remember that positive predictive value simply means that of the positive screens, half of those actually end up with an ASD diagnosis. In 1 large study reviewed, 18 989 children were screened with the M-CHAT/F and only 272 children or 1.4% continued to screen positive and were offered evaluations.^{3–7} If a busy pediatric

Corresponding Author: Craig M. Powell, MD, PhD, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-8813 (craig.powell@utsouthwestern.edu).

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practice screens 1000 toddlers each year, 14 patients would be sent for evaluation for ASD and roughly 7 would be diagnosed with ASD. Importantly, 5 of those 14 would receive a non-ASD diagnosis. Overall, the probability of identifying ASD, a non-ASD diagnosis, or a developmental concern with the M-CHAT/F is 98%. Very little is known regarding negative predictive value of these tests, so developmental surveillance and parental concerns continue to be important tools in spite of a negative M-CHAT/F result. The M-CHAT/F and M-CHAT-R/F are freely available online for all pediatricians and other health care professionals taking care of children. The initial screens can be done on paper forms or on computers in offices and take approximately 10 minutes. These initial screens can be given by personnel with minimal training.

If the goal of screening is to identify patients with ASD early, is there evidence that early treatment is effective? The short answer is yes, though more studies with longer-term follow-up measures are needed. In randomized clinical trials, some with blinded, objective outcome measures, significant positive results are achieved with a variety of behavioral therapeutic interventions in young children. Some studies even suggest that intervention at younger ages is associated with greater improvement.¹ Certainly our neuroscience-based understanding of developmental critical periods for brain plasticity imply that earlier is better, but interventions must be tailored to the child's particular developmental stage. Still, no studies have compared long-term outcomes in patients identified through screening compared with those identified, presumably later, by parental or health care professional concerns. Such studies along with head-to-head comparisons of early vs later behavioral interventions are needed. Most behavioral/developmental therapies incorporate aspects of applied behavioral analysis, play/interaction interventions, or parent training. We know too little regarding exactly which patients will benefit most from particular treatments or which treatments are better than others. The *JAMA* article¹ covers evidence for the best-studied interventions and provides a useful starting point for parents and professionals seeking knowledge about which therapeutic modalities to consider.

I anticipate that some in the lay press or other circles may misinterpret the conclusions of this evidence-based review as a death knell for autism screening. Nothing could be further from the truth. We support untrained parental screening for developmental concerns in all 50 states with little in the way of systematic evidence for or against. Parents and health care professionals are already screening for autism informally with even less evidence basis. In roughly 50% of pediatric practices, formal ASD screening is being performed, presumably allowing for earlier diagnosis and treatment. Early intervention can provide significant benefits, though it remains to be seen if such intervention is better than delayed therapy. Who among us would volunteer their child for the delayed diagnosis or delayed intervention group?

How do we move the field of ASD research forward in light of this systematic, evidence-based review of ASD screening and behavioral intervention? Generic calls for more and better studies and more funding for ASD research are warranted. We need to develop consensus on the goals of therapy. Do we target ASD core symptom domains such as language/communication and repetitive/restricted behaviors? Should we target intellectual ability as well? What are the most useful long-term outcome measures in terms of ASD—

diagnosis, social well-being, core symptoms, IQ? Goals of therapy need to be made in concert with patients, families, and ASD community organizations.

Autism spectrum disorder is one behavioral diagnosis with potentially hundreds of genetic, environmental, and gene/environment interaction causes. Future research needs to be aimed at understanding what goes wrong in the brain as a result of these insults and how these molecular, cellular, and developmental alterations can be improved or corrected with novel medical therapies. This is being accomplished through studies in patients, animal models, and human cellular models derived from induced, pluripotent stem cell research.⁸ Even if the resulting functional brain problems could be reversed completely pharmacologically or genetically, developmentally appropriate behavioral interventions will be needed to track patients back on to typical developmental trajectories that may have become derailed prior to treatment. As we identify specific genetic and environmental etiologies for autism, thorough phenotyping and natural history studies of such etiologically homogeneous patient populations should be performed to better inform future clinical trials. Genetically accurate animal models of ASD have been created, studied mechanistically, and successfully treated with pharmacologic and genetic approaches.⁸ Translating such novel treatments into successful clinical trials in concert with established behavioral interventions will provide a key to more successful treatments for autism in the future. Our goal today may not be to cure ASD, but rather to help patients and families reach their desired, optimal outcomes just as families with typically developing children work with society and educational systems to help their children reach their highest aspirations.

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