Autism: A Discussion With Experts

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Transcript of the Panel Discussion
as recorded on the Audio CD
Numbers indicate CD Track

1 Introduction

2 Dr. Hyman: My name is Susan Hyman. I’m a developmental pediatrician and an associate professor of pediatrics at the University of Rochester Golisano Children’s Hospital.

Dr. Baron-Cohen: My name is Simon Baron-Cohen, and I’m a professor of developmental psychopathology and also director of the Autism Research Centre at Cambridge University in England.

Dr. Rice: My name is Cathy Rice, and I’m a developmental psychologist and an epidemiologist at the Centers for Disease Control and Prevention.

3 Dr. Hyman: Autism is a very important topic for pediatricians, since we’re the first people who see very young children with autism, the first people that parents come to, and really the first people who often have any suspicion that something is different in development. I think it might be very helpful to talk about the scope of the problem.

Dr. Rice: A big concern lately has been: is the prevalence of autism increasing? We know that there are more people diagnosed with an autism spectrum disorder - where we see autism as one of a series of conditions that have a similarity — where, in the past, we tended to think just of autistic disorder or the more severe form of autism.

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4 Dr. Hyman: It might be useful to talk a little bit about what some of the symptoms of autism might be so that we can understand about this idea of a spectrum.

Dr. Rice: I think that’s a very good point for Dr. Baron-Cohen: Simon, you often say autism spectrum conditions versus disorders, and I think that brings up some very important questions about what is the “between” proclivity, a series of features versus a compilation of behaviors that comes to be seen as a disorder.

Now, when we’re talking about the autism spectrum disorders, generally we mean autistic disorder, pervasive developmental disorder not otherwise specified or atypical autism and Asperger disorder. All three of those conditions share a significant range of impairment in social interaction, in either awareness or interest in interacting with other people. Also, in common across the spectrum are unusual behaviors and interests and, in many people, particularly those with pervasive developmental disorder not otherwise specified (PDD-NOS) and autism, having delayed language and unusual communication.

The main difference for people with Asperger is that they tend to develop the basic parts of language, the using words, the communicating in sentences on time, but have a very difficult time with social communication. When do you talk to somebody? What kind of topic do you use? The pragmatics of how you communicate with somebody, as well as having average to above-average range of intelligence.

Simon, do you have anything to add?

5 Dr. Baron-Cohen: It’s interesting, Cathy, that you’ve started off talking about the diagnosis and the symptoms of autism spectrum in terms of social difficulties and also these unusual behaviors. But I guess the problem for clinicians is, where do you draw the line? At what point would you say a child has too little social interest or abnormalities in social interaction, because obviously there’s a lot of variation in any group of kids in terms of how sociable they are and what their interests are.

One of the issues surrounding diagnosis: is it a symptom? Is it a sign of a disorder if a child has an unusual pattern of interests, if they become fascinated by makes of cars or how the electric fan works? Okay, maybe most kids of that age are not focusing to that degree of detail in a particular topic, but is that a sign of pathology?

Dr. Rice: We have to look at the cluster of symptoms. I know a lot of people are concerned. So say as a pediatrician, you have a child who may be pointing in an unusual way; they’re pointing with their whole hand versus using a finger point. At what point does that become a concern? I think any single, discrete skill or any particular interest in and of itself is not a concern. Many of us have unusual degrees of intensity or interests and that’s what makes a lot of us academics who have gone to school for years and years, because we have a very obsessive focus with particular areas of learning. Those can be very positive skills. At what point does that cluster, together with impairments in social reciprocity and the ability to communicate, where a child is going to be limited in the ability to participate in typical activities or where the family is working so hard that their energy is being expended in a way that wouldn’t be considered typical?

Dr. Hyman: Cathy, I think that’s a very good point for
the primary care pediatrician who's on the front line to decide when it's unusual for a child to be interested in a cartoon character or playing cards and when it becomes clinically significant. So the idea of having ongoing surveillance and screening and the understanding that there are people in the community and within the education system, through early intervention for the 0- to 3-year-olds and through the school system for the 3- to 5-year-olds, who will assist in determining when is it clinically significant using standardized tools is really important to understand.

Dr. Baron-Cohen: We started talking about, is autism on the increase, autism spectrum on the increase? And I think that in the old days when we just focused on autistic disorder or classic autism, maybe this whole issue about when is a behavior abnormal was much easier, because if you had a young child who just never responded to, say, their mother's voice or to requests for communication, that they were so extreme in being cut off, then everybody would agree that this is abnormal and constitutes a problem.

But now we've widened their criteria to recognize milder cases. I think that's where the whole issue comes up about, are some people now being counted that never used to be counted? And are we sometimes giving a diagnosis to somebody who was just in that gray zone in previous years?

Dr. Hyman: Cathy, are the numbers increasing?

Dr. Rice: What's interesting is when you look at the few trend studies that look at the same population over time using the same methods, they tend to find that the increases are either at the ends of the spectrum, overlapping with the extremes of cognitive functioning, so those with severe, profound mental retardation (MR) or those with average to above average intelligence. It appears that the more moderate form of autism associated with mental retardation, typically what we would call more classic autism, appears not to be increasing at the same rates as the milder form or autism in the more severe form, which has led people to theorize that this is really the expansion of the diagnostic criteria and our recognition versus a true, underlying risk factor that only affects those ends of the spectrum.

We don't have the best evidence to say for sure, 100%, does diagnostic substitution, or does increased awareness, or does the application of a wider spectrum of criteria really account for the increase in people with autism, which we now believe affects about six per every 1,000 children. And a recent study, I think that was just done in England, looking at almost 1% of children in a community in England being identified with an autism spectrum disorder. That's much more prevalent than we thought.

Dr. Hyman: Cathy, you use the term diagnostic substitution. What does that mean?

Dr. Rice: Well, there's been an idea that you should be able to see decreases in other types of diagnoses, such as mental retardation, as you see increases in autism, and that's a very controversial topic. There have been people who have claimed, for instance, using data from the California Department of Developmental Disabilities Services. However, another analysis of the same data concluded that you did not see decreases in MR, as you saw increases in autism. So it's not clear-cut and it depends how you look at the data.

Another recent study by Paul Shattuck concluded that diagnostic substitution did appear to be happening, that you saw decreases in categories like learning disabilities, as you saw increases in autism. So that would point to the same type of kids with the same behaviors getting different labels than they did in the past.

Dr. Baron-Cohen: Cathy, do you think that there may be some incentives for parents to be pursuing a diagnosis on the autism spectrum for their child, which didn't previously exist?

Dr. Rice: Prior to early 1990s in the United States, there wasn't an autism eligibility category for special education services. Now, if you have an autism eligibility category for school, you're more likely to have more flexibility in your special education services. There are statewide programs and local programs that target autism that didn't in the past.

Dr. Baron-Cohen: So one possibility is that parents are actually pushing more to get their child diagnosed because the child then gets the right support and that just wasn't there before.

Dr. Rice: Yes. I definitely think that's a change. Whether that push is appropriate or not is still up in the air because I think what we found in the past is that there were many children who were undiagnosed that should have been, and parents found that even when their child had a severe form of autism, even though they brought their concerns to their healthcare provider early on, there was
of when that child actually got an appropriate diagnosis. So I think the parents push and interest has been very important. And it’s something that, at the Centers for Disease Control and Prevention (CDC), we’ve actually encouraged through the Learn the Signs, Act Early campaign of trying to get families and healthcare providers, daycare providers, to pay attention to the signs of development that we don’t usually pay as much of attention to. Not just height and talking, but playing, communicating, those types of things.

Dr. Hyman: In addition to the change in the educational law, there are some other things that happened in the late 1980s and early 1990s, including the early intervention legislation, so that children age 0 to 3 years in the United States got services, but there was also the publication of Dr. Lovaas’ landmark article about behavioral treatment. So there was the perception, if not the reality, that there was something you could do to modify outcome.

Dr. Baron-Cohen: Yes. I’m sure you’re right that just knowing that autism is treatable, let’s put it that way.

Dr. Hyman: But not curable.

Dr. Baron-Cohen: Not curable, but that certain interventions do make a difference. Just knowing that might, first of all, have changed the whole image of autism. We used to think of it as a devastating disorder, whereas now there’s a much more positive view that some children are slower to develop in social communication and with the right intervention, they can make gains. So I’m sure that’s also helping to bring parents forward to have their child recognized.

Another significant publication, which happened in the early 1990s, late 1980s, where simply just the inclusion of Asperger syndrome in the classification systems, whether it’s Diagnostic and Statistical Manual (DSM) or International Classification of Disease (ICD), and many books being written, many articles being written about that subgroup on the autistic spectrum.

Dr. Rice: Right. I think that’s very important, particularly when we look at prevalence over time, because those may be individuals that we weren’t counting in the past, and it’s very challenging to go back retrospectively. Autism is considered a lifelong disability. There are children who may, through intervention or just through development, grow out of their symptoms, but that’s considered extremely rare, and we don’t really have good data to support that that happens very often.

However, we really don’t know what those individuals look like as adults, but I know anecdotally. I know individuals, certainly, who clearly qualify for a diagnosis of Asperger or high-functioning autism now who were not identified until adulthood, and that is relatively common. How you actually do a population screen to capture all of those adult individuals is quite a challenge. The studies that have been done look at institutionalized populations, which is a problem for identifying people with Asperger, because here you have bright, verbal people who may have significant social adaptive impairments, but are probably not to the level of institutionalization or, if they are, it may be for mood disorders.

Dr. Hyman: What you’re bringing up, Cathy, is an excellent point about this idea of a spectrum of symptoms. And Simon, some of the work you’ve done addresses this idea that you can have little bits of autism but be below the threshold for diagnosis.

Dr. Baron-Cohen: That’s right. Cathy has raised the whole question about very late diagnosis; that’s to say, individuals who got through their childhood and adolescence without a diagnosis, but by young adulthood, they may well be seeking a diagnosis. So this is the Asperger end of the spectrum, and we don’t have good tools for making those assessments in adulthood. Many of the tools have really been developed for young children.

Dr. Rice: Or have only recently been developed.

Dr. Baron-Cohen: Sure. Autism isn’t a simple disease like other diseases. Whereas with a straightforward disease, we would say that it always causes problems and the individual would be better off without it; in fact, society would be better off if that disease was eradicated. In the case of autism, it’s much more complicated because one-half of autism involves disability, but the other half can involve areas of strength. What we sometimes pejoratively call obsessions, you could, in a neutral fashion, just call strong interests in a narrow topic, and those strong interests can sometimes lead to great contributions or specialization.

So we need to be careful that we’re not simply treating autism like any disease that needs to be prevented and cured, because some of those individuals don’t necessar-
Ily want a cure. They don’t want to be eradicated. They just simply want support for their areas of difficulty, but otherwise have their areas of difference and even strength valued.

**Dr. Rice:** I find it very challenging because you have two extreme passionate groups. One tends to be the parents of young children, often with more severe autism, who may have very debilitating associated conditions, like sleep problems, gastrointestinal problems, self-injury, aggression, where these families lives are very, very stressful, very challenging. All they can think about is a cure and, it’s understandable.

On the other end, you have, particularly, the adults who can speak for themselves, who may have much milder forms, may have lots of challenges, but can focus on their strengths as well.

**Dr. Hyman:** Autism is not a discrete entity. It comes from multiple genes interacting with each other and probably with environmental events that we don’t yet understand, which explains why there’s such heterogeneity, difference between individuals. And even within the same family, you can have some individuals who have Asperger syndrome or high-functioning autism, and other individuals who have severe cognitive limitations. So I think that the heterogeneity, variation of symptoms within the spectrum is something that we need to acknowledge and that there’s no single treatment that you can use to address all of the symptoms. What’s key is identifying the disorder or the condition early, so that appropriate interventions can be applied. And before we talk about some of the specific interventions, it might be useful to talk about the idea of early identification and early diagnosis, both for lower and higher functioning individuals.

**Dr. Rice:** The American Academy of Pediatrics (AAP) has come out with some very useful tools, like the policy statement for surveillance and screening in the medical home that has a very nice algorithm of certain points during the well-child visits where general developmental screenings should be undertaken in addition to your routine developmental surveillance. You’re trying to get at whether there are concerns at the certain checkpoints doing a standardized developmental screening assessment and, at certain test points, there will be some additional recommendations — Sue, you can talk about that a little bit more specific to autism — coming out in 2007, along with a toolkit, to help in terms of getting access to autism-specific screening tools and time points, particularly at 18 months, ideally 24 months, and potentially 30 months of age, too, where specific screening for autism is done.

**Dr. Hyman:** Cathy, you’re absolutely right that generalized developmental screening is critically important to identify language, motor, and cognitive delays. General developmental screening using a standard instrument is not specific for autism. In fact, some of your work, Simon, years ago has really been at the forefront of identifying what the earliest symptoms are that a pediatrician might see.

**Dr. Baron-Cohen:** Yes. We focused on children at 18 months old because, at that point, there are some clear behaviors that should be present and, what you’re after, neither reduced or absent in a child who’s going to go on to receive a diagnosis. Examples of behaviors like that are joint attention. The normal range for establishing joint attention is 9 to 14 months of age.

Joint attention are those behaviors that bring the infant into a shared focus with another person. In concrete terms, it would be looking at somebody else’s face, at their eyes, and when they turn to look at something, you follow their gaze and look in the same direction. That would be one example of joint attention.

A second example would be the pointing gesture, where the infant would either produce a point and, at the same time, making eye contact to see that it’s being received by another person, or else they would follow a point that, say, the parent is pointing at an object with the index finger. The infant doesn’t just look at the finger, but they look across to see where the finger is pointing and, again, an exchange of eye contact to show that the message is being received, that there’s some shared interest in the topic. All of that is before language. It’s preverbal communication.

**Dr. Rice:** I think that’s a really important point for early identification of autism because, for so long, we focused on the verbal language aspects of autism that individuals are nonverbal or when they do become verbal, they use a lot of echolalia or stereotyped language. Now we have a conception that people can be hyperverbal and very verbal and still have autism. But beyond that, it’s more about a communication issue. It’s about the nonverbal communication as well, and joint attention is a crucial part of that. How are you following other people’s nonverbal communication, as well as using it yourself? Some of the important things are, is the child between 12 and 18 months? Are they beginning to point to show you things, not just to have the parent get them something?
So those aspects of joint attention and nonverbal communication are important as well.

Dr. Hyman: That’s right, Cathy, and these symptoms are all developmentally graded so that, in a very young child, joint attention may have to do with eye gaze and pointing. By the time you get to school age or in a child who’s hyperverbal, what you may see is someone who is interested in lecturing you about their favorite topic, be it dinosaurs, or trains, or electric fans, and not really interested in the turn-taking aspect or the idea that other people have a different point of view in understanding language. So the pediatrician does need to be aware that it’s not a single concept, but a broad set of core symptoms that may look different at different ages.

Dr. Baron-Cohen: Sure. I mean even in this conversation we’re having right now, there are three of us in the room and we’re all trying to take turns and look at each other in order to check if the other person wants to come in on the conversation, and we’re trying to establish a common topic to make sure that we’re actually all communicating about the same thing. And I think that’s precisely what you see preverbally when the infant is pointing and checking the other person’s face and knowing when to come in or when to stop. So you’re right; you can’t just focus on the surface behavior. You have to focus on what’s underlying it.

Dr. Rice: Right, and a lot of times in autism, it’s not the discrete behavior. It’s the context of it. So for instance, pointing. We can say, “Oh, yes. Johnny points,” but again you have to look at the content. Are they pointing to get something or are they pointing to show, which is a much more social behavior.

15 Dr. Hyman: An interesting question now in our multicultural society — are some of these communicative behaviors altered by experience or altered by culture?

Dr. Baron-Cohen: Anecdotally, we might think of one culture being much more sociable than another. We think of stereotypes between different nations, that some are much more communicative than others. But I think what the studies show is that whichever culture you look at, children do establish joint attention. So we may not know much about the quantitative differences between cultures, but we do know that wherever you study 18-month-old children, they look at faces, they follow gaze, and they point.

Some cultures actively discourage pointing. They think it’s rude, but just the very fact that human infants spontaneously do it, even if their culture then sanctions it or doesn’t, shows that there’s a partly biological or universal aspect to this line of child development.

16 Dr. Rice: There are other really important early signs that pediatricians can look for in terms of indicators of when should you — as part of your development surveillance, if these issues come up — when do you institute a developmental screening and then go to the next step for an autism screening? And some of those are: pointing, as we talked about, no pointing by 1 year of age; no babbling by 1 year, or single words by 16 months; no two-word phrases by 24 months; using repetitive or echoic speech; no response to name when called without a hearing loss. So a lot of times you find families are first concerned that their child has a hearing impairment and upon further investigation of hearing, find there’s really not a problem there. It’s more a differential social responsiveness.

Looking at a loss of language or skills, at any time you see a regression — not just “my child is a little bit whiny or needs his blankie a little bit more for a day or two,” but a genuine regression of a child who’s using language functionally and then those words disappear — that’s an important red flag. Little or no eye contact or other gestures like head shaking or nodding, limited interest in other people or watching other children, little interest in making friends or imitating other’s behavior, and no pretend play — I think all of these are some key items and they crossover with the Checklist for Autism in Toddlers (CHAT) and the Modified Checklist for Autism in Toddlers (M-CHAT), with some of the screening instruments that, Simon, you might be able to talk a little bit more about.

Dr. Baron-Cohen: To me, one of the more unusual items on that list is the pretend play item, because why is pretend play important? If we think about, say, an 18-month-old who might be engaged in pretend play with their parent, the parent may be doing something quite bizarre like kissing a doll that the child is playing with, pretending that it’s alive. And whereas a typically developing child will make sense of that behavior and understand that the parent is just pretending or injecting something imaginative into the play, what we know is that children with autism find that less interesting, that pretend just doesn’t carry the same interest or may even be confused by that kind of behavior. So the absence or reduced interest in pretend play can also be a strong predictor.
17 **Dr. Hyman:** These behaviors are also neurologically based. What we understand about the emerging neurobiology of autism would suggest, for example, that imitation might be abnormal because of the difficult or abnormal connectivity in the brain between seeing and being able to produce what you see on a motor basis, so that treatment may involve practice and may involve building up alternative strategies. We may never be able to overcome some things that are hardwired differences; and some of the things that we’re talking about in terms of echoic speech, for example, and perseveration, some of those may reflect hardwiring differences and some of those may reflect our response to social anxiety or not understanding the language or intent of others. So understanding why behaviors occur may help us bridge towards treatment and management.

**Dr. Rice:** I think that’s a really good point because people say, “Well, what’s the advantage of knowing that autism is the condition you’re talking about?” I think that’s very helpful for targeting treatment. I tend to think of autism as being these very selective skill sets, of using components of your brain just singly focused versus being able to connect, or have the connectivity that requires a valuation of different skill sets across your mind. In some ways, that speaks to the difficulty people with autism have in generalizing, have with certain types of abstract thought. Why do people with autism learn certain skills very well in one setting, but the same skill is a mystery when you go from home to school? That transfer in that way and how the brain works, Simon, you’ve done a lot of work on the neurobiology of autism.

18 **Dr. Baron-Cohen:** Just going back to this question about imitation and echolalia, echoing speech, echoing behavior, and also perseveration. It’s interesting that you could take any one of these symptoms and when you start to analyze it, you realize it’s really not very straightforward. So perseveration, that could be a sign of some neurological problem, that they just can’t shift their attention; and maybe some frontal lobe abnormality, sometimes called an executive dysfunction, that they’re stuck in a loop and repeating their behavior. But another interpretation of exactly the same behavior is that the child finds it easier to keep repeating because then there’s predictability, whereas in the social world, of course, things aren’t very predictable. Things don’t repeat. You can never really anticipate what’s going to come next because people aren’t scripted in their behavior. So the one symptom could be interpreted neurologically in one way, or it could actually just be a sign of the child’s difficulties in making sense of the social world.

**Dr. Rice:** We’ve talked about some of the early signs and using some of the screening tools, which may include the M-CHAT or the CHAT, the Checklist for Autism in Toddlers, or the Modified Checklist for Autism in Toddlers. There’s also the Screening Tool for Autism in 2-Year-Olds (STAT) and the Pervasive Developmental Disorders Screening Test (PDDST), which are useful tools after doing your first-line developmental screening with something like the Parents’ Evaluation of Developmental Status (PEDS) or the Child Development Inventories or Ages and Stages Questionnaire.

19 But the key is, once you have a suspicion of a developmental concern, I think we should talk a little bit more about what, as a pediatrician, would you do next?

**Dr. Hyman:** In every state of the union, there are early intervention programs for children 0 to 3 years of age. The pediatrician can refer for a developmental assessment and early intervention is responsible for providing intervention for children at high risk for disability. There is diagnostic overlap between multiple types of disabilities. It’s very important to look at general development, as well as autism-specific symptomatology. So for children 0 to 3 years, the referral is to early intervention. For children 3 to 21 years in the United States, your referral for intervention is through the school system.

**Dr. Rice:** Right, and then you may have to consider each community is different in terms of other state or private resources that are available. So as a pediatrician, it’s hard to give any generic rules of thumb beyond the early intervention and the public school system because it does really vary in a community-specific way.

**Dr. Hyman:** And Cathy, the keyword is early.

**Dr. Rice:** Yes.

**Dr. Hyman:** Whether or not you have a higher functioning child who you would like to have social-skills interventions in a school-age or a younger child, the earliest time of identifying these true neurobiologic and social differences will make a difference in terms of appropriateness of intervention, and also appropriateness for the family to understand that repeating the same conversation over and over again may not be just oppositional behavior, but may be this need for predictability and social anxiety management. The keyword is early; the earliest that you can identify concerns, you can get the family and the child into appropriate intervention and also make sense of some of the other symptoms that
you might see that aren’t core symptoms of autism. But certainly, children with autism who have sleeping and eating and other compliance issues, they’re like all other children, but just more so.

Dr. Baron-Cohen: One aspect of early invention we haven’t really touched on is the benefit, not just for the child, but for the whole family, because if you have a child who is really quite challenging, that can come to dominate family life and cause a lot of stress for parents and siblings. So early intervention could also just lead to a calming down at home, because suddenly the difficult behavior can be managed and parents can start getting answers to what otherwise seemed to be mysterious aspects of their child’s behavior.

Dr. Rice: One of the challenges, a lot of times we say, “Why are families of children with autism so intense to some degree?” And part of that is the nature of the disability they’ve been dealing with, because it’s not clear-cut. There’s not a physical sign. There’s not a biological test that says, “Ah-ha. Your child has a disability.” So the parent has been struggling with the child who’s got these unusual skills, some strengths and some weaknesses, that add up to a very confusing picture and often they are the ones who are pushing forward for a diagnosis. The family has to go through a period of grieving and adjustment. And really, appropriate intervention means treating the whole family.

Sue, do you have any other comments in terms of appropriate intervention and what that is?

Dr. Hyman: Yes. One of the things that parents will often ask their pediatricians is, how many hours of service should I have? What sort of service should I have? Should I get occupational therapy? Should I get other additional therapies? In the absence of data, it’s very hard to advise people about specific interventions.

What we do know is that therapy that’s provided early, provided intensely, and generalized to the home setting is likely to effect the most change. The National Academy of Science put together a wonderful review document in 2001 that identified that the commonalities of disorder-specific treatment programs; in other words, treatment programs that recognized the core differences in autism are more similar than they are different. They require developmental appreciation of needs, specific addressing of core differences in learning social language, and involvement of the families so that these interventions can be generalized.

There are certainly lots of camps regarding one therapy being superior than another. There are limited data regarding the optimal therapy for individual children, and availability of different types of therapies varies across the country.

Dr. Rice: Yes. I think it’s also amazing how poor we are at predicting what child will respond best to therapy. We’re really at a point where studies that look at individual child characteristics as a way to channel them to the most appropriate therapy are really just beginning now, and that’s going to be a very important area of research.

Dr. Baron-Cohen: Yes. I was going to come back to something you said earlier, Cathy, which was about there is no physical test for autism, because obviously that makes diagnosis much harder compared to other conditions, but it also links to what Susan was saying about how autism is a neurological disorder.

Maybe we should touch a little bit on some of the recent findings really demonstrating once and for all that autism is the result of atypical brain development. It has been an important step forward to be able to really demonstrate, using some of the new imaging techniques, brain scanning techniques, that there are differences in the way the child’s brain is developing and functioning.

Dr. Rice: Right, and one of the many paradoxes of autism is that it is a biological, neurobiological disorder that is treated through educational or behavioral means. So as a medical provider, people are coming to you for answers, and there only are so many answers at this point.

Dr. Hyman: Simon, maybe you could comment a little bit on some of the very exciting functional imaging technologies that give us a window on the brain.

Dr. Baron-Cohen: Sure. Functional magnetic resonance imaging (MRI) now allows us to look at the brain whilst the person is doing a task, and we can compare groups of people with autism to groups without autism. Some examples of findings that have come out quite consistently over the last few years: there’s a region in the limbic system, the amygdala, which is either underactive whilst the person is, for example, looking at faces, looking at emotional expressions. The brain in the people with autism seems to be underactive in this region, the amygdala. But also when you look at the structure, because MRI allows you to measure the size of different structures, the amygdala has come out to be atypical in size. In
some studies, it’s too big. In others, it was too small. But certainly we’re getting a message from these studies that the development of this part of the brain, which people think of as the emotion center, is not developing in the usual way in these children.

That’s just focusing on one little part of the brain. But there are other studies showing that overall brain volume is also — the rate of growth of the brain is also atypical. And there has been some interesting recent work showing that a proportion of children with autism have large heads, and this corresponds to larger brains, maybe about 30% of kids with a diagnosis. So these don’t allow us to rely on the physical test for diagnosis because none of these findings are true of all autistic kids. But they are certainly telling us that neurodevelopmental patterns are different in this group.

24 Dr. Rice: And I think it’s useful for pediatricians, in terms of the typical clinical workup that you would do, of measuring head circumference — where for children with autism, you may not find an increased head circumference very early on, but you see an increase in the toddler ages and then more verging back towards typicality.

Dr. Hyman: That is correct. The clinical report that the academy published in *Pediatrics* in 2001 is going to be reevaluated for publication in 2007. The diagnosis of autism is a clinical diagnosis. The screening tests and diagnostic tests are behaviorally based in terms of what you see and what you can elicit, but the ultimate diagnosis depends on *ICD-10* or *DSM-IV* criteria. The screening tests and other measures support application of *DSM-IV* criteria. Although we do not have a biologic test that is diagnostic, we need to think about every child who has a developmental disability, especially in the context of autism, for what else might be associated.

And there certainly are other genetic disorders that are associated with autism. So every child who we think might have autism needs to have their physician look at their skin to make certain they don’t have tuberous sclerosis since there’s a significant association. So you need to look for ash-leaf spots and adenoma sebaceum, and doing it in the newborn period isn’t adequate because the skin symptoms can emerge over time. Similarly, you need to do a good neurologic exam to make certain that you’re not dealing with an underlying set of neurologic systems that require further evaluation.

There’s a comorbidity or a co-occurrence of autism with fragile X syndrome, so if you have unexplained cognitive limitation, doing specific DNA test for fragile X syndrome is warranted. And indeed, you need to do a very careful history and physical. That’s the indicated medical workup at this point to determine whether you have reason to suspect seizures, which up to a quarter of children with autism might have sometime in their lives. A focal neurologic exam or an unusual history might make you want to look further at conventional neuroimaging.

25 Dr. Baron-Cohen: What I find very confusing is that we have got lots of old data, for example, telling us that a quarter of children with autism will also have epilepsy at some point in their lives, but that is old data. I mean, it comes from the 1970s and 1980s. And now that we’re recognizing the so-called high-functioning end of the spectrum and Asperger syndrome, I’m not sure, with our hands on our hearts, we can tell parents what the current statistics are on things like associations with epilepsy. Is it really as high as 25% anymore or, in the Asperger group, maybe it’s much, much lower than that.

Dr. Rice: We found at CDC, through our prevalence studies, being around 8% co-occurrence, but we really think that’s a minimal estimate because it’s what was documented in the children’s often educational and medical records. We do have a project that is looking at the co-occurrence of epilepsy and autism, and hopefully they’ll have findings to report next year. But I think that’s an important point.

26 Dr. Baron-Cohen: The same thing applies, of course, to what in the States you call mental retardation and, in England, we call learning difficulties, but below-average IQ. And in the old days, we used to say three quarters of children with autism had below-average IQ. But what’s the true figure today?

Dr. Rice: Right. It’s quite a range. You have some studies that show as few as 25% of individuals with autism having associated mental retardation. The average seems to be closer to 50% in the variety of studies that have been done recently. So that’s a very different population than when we were talking about autism, you were talking about three-quarters most likely have mental retardation as well. Now we’re talking about 50/50 chance, and that’s very different in terms of the learning abilities, needs, trajectory of those individuals.

27 Dr. Hyman: You can say the same thing about other associated medical problems. Many families are quite quick to point out that gastrointestinal problems are seen somewhere from all to most children with autism, but we really have no idea what the scope of the problem is. So the scope of the problem really needs to be defined.
Dr. Baron-Cohen: What’s good about that last point is that it reminds us that autism, although it’s defined in terms of social difficulties, the biggest problem for a family may not be the social one. It could be something like, “my child is in pain through digestive problems, and that the social problems are minor compared to the fact that my child is screaming every time he or she needs to go to the bathroom.” So these gastrointestinal (GI) issues may, for some families, be right at the center.

28 Dr. Hyman: And pediatricians may find that in very young children, concerns about discomfort, sleep problems, and concerns about GI problems like feeding and not feeding really have primacy for families. Above all, children with autism are just children and if a parent comes in complaining of constipation or GI distress or vomiting, that we need to work these children up the way that we would work up anyone else who comes in with similar sets of problems. At this point in time, we don’t have evidence of a primary gastrointestinal abnormality in children with autism, but you can’t ignore symptoms.

Dr. Rice: I think that points out the balance of medical intervention versus behavioral intervention. Where do you draw the line for autism in terms of treatment? And a lot of times I think we would take associated conditions and say, “Oh, that’s just part of the autism,” and not treat the child as a typical child. I think that’s a really important point about investigating potential medical causes that you can do something about or those that you can’t; and you also need to do behavioral intervention as well or in conjunction with each other.

29 Dr. Hyman: Cathy, we can use feeding and sleeping as examples. These may be problems that are more frequent in very young children, but persist through the lifespan of children with autism. Children with autism may have intensification of the pickiness that other young children have in terms of food selectivity. They may or may not actually have a greater frequency of food selectivity, but maybe more selective. It may be part of the underlying neurobiologic disorder in terms of obsession. It may be behavioral in that parents don’t use the techniques they would use with their other children to expand the diet, or there may be other physiologic things related to primary differences in taste or smell or other aspects of the food, which make the child have a negative reinforcement or a punishment for eating things that make them feel ill.

Dr. Baron-Cohen: Yes. The issues around eating are sometimes the ones that come to parents’ attention and may be the reasons why the child ends up seeing a doctor, but they may simply be part and parcel of this hyper-sensitivity to stimuli right across the environment. So the child with autism who finds lights too bright, or sounds too loud, or textures that they have unusual preferences for — those things may not be sufficient to cause alarm. Whereas when you have a child who’s really restricted the diet to just one type of pasta and the parent can’t really shift the child into eating a range of foods, that may just be an indication that the child is very picky in terms of which stimuli they find easier or more difficult.

30 Dr. Hyman: Another problem that’s very prominent in young children is sleep dysfunction. Sleep certainly is responsible for a lot of general pediatric visits with or without autism. Among children with autism spectrum disorders, they may well have a biologic reason for difference in terms of melatonin secretion during the night to regulate the day/night cycle. They may well have a difference in terms of the neurophysiologic regulation of sleep state that you can see on polysomnography. But you also may have the core differences related to autism not discriminating day and night or perhaps being reinforced by interaction with the parent in a less-stimulating time of day.

Dr. Baron-Cohen: You know, you have to wonder how much of this is social and conventional and how much is purely biological. So, you know, we have it in our culture that we go to sleep at night and you wake up in the morning. And a lot of that may be reinforced as part of our culture. Obviously there are these rhythms, which may not be anything to do with culture.

When we see adults with Asperger in our clinic, it’s very often the case that they just report that they prefer to be nocturnal. That when everybody else is asleep, they’re at their computer until the small hours of the night. The parents wonder why they’re still asleep at 3:00 in the afternoon, but they’ve just shifted their whole pattern. And then you wonder whether that’s got anything to do with avoiding the social contact because, of course, if you’re awake at night, you have less social contact. And if you sleep in the day, you can avoid social contact. So again, you can take a single symptom and realize that there may be lots of contributory factors.

31 Dr. Rice: On a broader level, some of the challenges of what the family is dealing with are the recurrence rates of about 3% to 7% of families that have one child with autism are likely to have a second child with autism.
Now it’s important to keep in mind that those statistics are more, like we were talking about before, basically older statistics looking at the individuals with autistic disorder, not necessarily reflecting the entire spectrum. There’s some indication that, in the broader spectrum, you may have increased family members who have sort of the broader autism phenotype, not necessarily the full-blown syndrome of autism spectrum disorder. So I think it’s important, in terms of early surveillance, that if you have a family that has one child with autism, you take a heightened level of awareness to look at the other siblings as well, looking for signs of autism and helping that family identify if there are learning needs in those other children as well.

**Dr. Baron-Cohen:** Much harder to diagnose the broader phenotype because that’s really where we’re blending into the general population, so it’s much harder to have a cutoff, if you like. But I agree that just the recurrence rate amongst siblings, even if we’re talking about classic autism, points to genetic factors. Genetics is going to be the eventual explanation for at least part of the explanation for autism spectrum.

**Dr. Hyman:** We have genes for everything. We have genes for language. We have genes for nail biting. We have genes for bedwetting. The autism phenotype seems to be a conglomeration of genes for individual traits that come together in any given person and are modified, perhaps, or turned on or turned off early in development by the presence or absence of other factors.

**Dr. Rice:** Right, and although inheritability is a significant factor, that’s certainly not the only way that genes could be interacting. And most likely in the case of autism, you do have a complex, genetic interaction with the potential environmental interaction, and I think that’s a big concern of what might that environmental interaction that creates autism be.

**Dr. Baron-Cohen:** Yes. We know that there will turn out to be an environmental factor because the inheritability, whilst it’s high, is not 100%. So there’s got to be some room for some interaction with the environment.

**Dr. Hyman:** The pediatricians get asked, “Is it something that I ate? Is it something that I drank, or is it something that you injected into my child that caused the autism?” There have been lots of epidemiologic studies.

**Dr. Rice:** There’s been a lot of epidemiologic studies, but they often don’t have very consistent findings. Part of the consistent finding is that there’s often a suboptimal either prenatal or perinatal period; but there’s not been one specific event that has been consistent across all cases of autism or even across the studies. I think, at this point, that’s pretty much what we know, and we need to follow individual families prospectively over a period of time and have a better understanding of exposures during pregnancy, family histories, various medications, those types of things, to have a better idea of the potential predisposition and potential exposures that may relate to a child having autism versus another disability versus no disability.

**Dr. Baron-Cohen:** And that kind of research is very much needed, and it may be that the CDC is in the best position to collect a lot of these environmental variables. But obviously the other side to it is parents worrying about whether they are in some way to blame for having not given their child the right environment, or taken some drug during pregnancy, or whatever. But I’m sure that’s just part of the natural tendency for parents to feel that they perhaps should take different steps that they didn’t. I think clinicians can go a long way to reassuring parents that, at the moment, we don’t have any good evidence that there were environmental factors that were under the parents’ control, for example, which may have increased the risk of their child developing autism.

**Dr. Hyman:** And we certainly don’t have evidence to date that the rate of autism changed with the introduction of the measles-mumps-rubella (MMR) vaccine.

**Dr. Baron-Cohen:** No.

**Dr. Hyman:** The recommendation of the academy at this point is to protect children from infectious diseases as best as we can.

**Dr. Rice:** Right, and certainly, of course, there’s a lot of concern about the role of vaccines and autism. I think, as you said, it is very challenging when you have families that are very convinced that there’s a relationship, potentially, between something like a particular vaccine and their child as having autism, which is a popular theory right now. But there are lots and lots of families who have heard that and they have also heard from the healthcare professionals that there really aren’t the studies to support it. The evidence at this point has shown that the vaccinations like the MMR have been safe and effective for children. So I think it’s important, as a pediatrician, that you can provide the evidence and the information to those families, especially those that are on the fence,
to say, “As far as we know, these vaccinations are safe and effective and have not been related to autism.”

35 Dr. Hyman: There are certainly lots of other theories related to both causation and treatment in autism, and many of these theories have resulted in novel treatments that may come from outside the medical profession. Some of these novel theories have to do with infectious causes of autism, autoimmune or other immune causes of autism, and other nutritional or physiologic imbalances. And at this point in time, we really have no evidence that additional workups, looking at either immune or nutritional factors, have a role in the initial workup or, at this point, we don’t have evidence regarding treatment.

The only strongly evidenced based treatment we have is behaviorally based intervention of an educational nature. There’s a tremendous amount of information available to physicians and parents regarding an ever-widening number of treatments that pediatricians need to be able to dialog with their families about. We may not agree on the appropriate interventions, but we need to recognize the situation that families are in and their desire to leave no i un-dotted and no j uncrossed in their search for improvement in their child’s outcome.

Dr. Baron-Cohen: Yes, and all of this is really reminding us that we need more research into evidence-based treatment because families are going to be prone to pursuing any new treatment that comes along, for all the best reasons in the world. They want to do the best for their child. But it means that if, for commercial interests, someone is pushing a new treatment that hasn’t yet been properly evaluated, those families could end up either spending money inappropriately or, in the worst case, putting their child through a treatment regimen where there are side effects.

36 Dr. Hyman: I would make a case that all treatments need to be evaluated with evidence. Whether it is an atypical neuroleptic drug that we might prescribe for stereotyped or repetitive behavior, or whether it’s a nutritional treatment that’s prescribed for stereotyped repetitive behavior. Atypical neuroleptics, risperidone in particular, have been very well studied, but not all medicines have by any means.

I would urge families and providers to identify their target symptoms that they wish to treat and to follow these symptoms prospectively, to institute treatments in a stepwise and systematic fashion so that no harm is done. Just like with medications that you can get by prescription, there are all sorts of things that you can get without prescription that may well have side effects.

Dr. Rice: That’s very important because I think there is an idea that the medical community has shut down to considering other treatments, but it’s not like we have the magic intervention. What we do know is that behavioral treatment should form the basis of other treatments, but that any other treatment, even behavioral intervention, always has to be looked at, weighing the costs and benefits, and that keeping the target symptoms in mind and, as a professional, helping the family evaluate those symptoms and the safety precautions, I think, are extremely important.

So, we’ve talked about a lot of the sort of the statistics of autism, and one of the most common statistics is that more boys than girls have autism; so we do need to have an increased, heightened awareness in terms of looking for features of autism in boys. But what do we know about — what does that mean in terms of etiology?

Dr. Baron-Cohen: Well, certainly people are really looking at the connection between your sex and your risk of a diagnosis. It’s opening up a whole bunch of candidate biological mechanisms that might play a causal role. So there might be sex-linked genes, and those need to be tested. But equally, there may be hormonal factors like testosterone, specifically fetal testosterone, which we know plays a role in shaping the brain towards either a typical male or a typical female. At this point, that kind of research is very much just research. It’s not yet at the stage where it would have clear treatment implications.

Dr. Rice: But it’s an interesting theory to look at and that you’ve done a lot of work on and been the champion for — this theory in terms of explaining some of the behavioral features that we see in autism and how that might actually relate back to the biology related to sex. How does that relate for autism?

Dr. Baron-Cohen: One way it relates is that if you look at typical sex differences — which obviously is a politically controversial thing to do, but parents recognize these differences — that, on average, little boys get very fascinated by things like toy vehicles and spinning wheels and so forth. So one possibility is that autism is just an extreme of the typical pattern that you see in little boys anyway. If you took it all the way, that playing with a little toy car might attract many boys, but playing with it for 3 hours and just having a very close-up focus on the wheels of that toy car may start to resemble autism. So is it just a matter of degree?
Dr. Hyman: One of the very exciting things about your research, Simon, is that it targets this very early period of gestation. You can see symptoms that emerge later in childhood based on neurologic events that happen during embryologic development.

Dr. Baron-Cohen: That’s right. And we know that there’s a surge in the production of testosterone by the fetus between about 12 and 18 weeks’ gestation. Some people think that that has an organizing affect on later brain development and actually sets the path of brain development. So it’s not just a window into development, but it’s also a sensitive period. Once events have happened of the hormonal kind during pregnancy, the child is going to be on one path rather than another for later brain development.

Dr. Hyman: Certainly children with autism spectrum disorders can have symptoms of inattention and impulsivity. They can have symptoms of obsession. They can have mood disturbances, and all of these may be at greater frequency than in the general population. As we talked about earlier, behavioral interventions are the primary focus of treatment. However, medications that we would conventionally use to address these symptoms may be very important in allowing these behavioral interventions to work.

There’s very good data that suggest that children with autism spectrum disorders can respond to the same medicines we use to treat inattention and impulsivity in other children, and there is very good data to indicate that atypical neuroleptics like risperidone may have utility in the context of an overall program for treating aggressive and disruptive behavior and stereotyped behavior. There are many other medications that are on the horizon that do not yet have the evidence to support generalized use, but we have reason to be excited about neuropharmacologic options in the future that may address core symptoms of autism.

Dr. Rice: And I think that’s important because, a lot of times, we may not think of particular medication because we’re trying right now to go to the core features of autism and to treat those. But looking at those specific behaviors that may be treatable is very important, as well as it does bring up a challenge of integrating symptom-specific medication use or other invention in children with autism. Along with their whole behavioral and whole spectrum of therapeutic programs that that child may have ongoing, the medication use may be just one piece of a whole program.

Dr. Hyman: An example could be the idea of inattention. School-age children with academic skills may come into your office because the teacher says they can’t pay attention, but what you have to tease apart is, are they not paying attention because of distractibility from environmental events, or are they not paying attention because they can’t? They’re scripting their cartoons in their head and perseverating. Or are they not paying attention because they can’t attend to the work as it’s being presented to them? The comorbidity with learning disabilities may preclude them from paying attention, so it’s not as straightforward as we might initially present.

Dr. Rice: I’m going to switch back to a topic we were talking about before, which was the need for research. We certainly know that if we’re talking about a condition that affects approximately six per 1,000 children, most pediatricians are highly likely to see a child with autism, or many children with autism, in their practice. And we have a long way to go in terms of really understanding the causes, the course, the intervention, and the lifelong needs for individuals with autism.

We focus a lot on early identification because that’s something we can do. We know we can have a positive effect on children’s development by identifying autism early on, but there’s a lot more research that needs to be done. I just wanted to mention earlier, when we were talking about risk factors, the Centers for Disease Control is about to start a multisite study of looking at early risk factors for autism called the National CADDRE (Centers for Autism and Developmental Disabilities Research and Epidemiology) Study, but there’s a lot of great research going on through the National Institutes of Health (NIH)-supported networks.

But if people are interested in learning more about the whole portfolio of autism research, you could go to the National Institute of Mental Health Web site, looking for the Interagency Autism Coordinating Committee, the IACC. They’ve put together a comprehensive research matrix that looks at the needs for autism research, in particular, more on the basic research end. But it’s a very nice roadmap to seeing where we are and where we need to go (http://www.nimh.nih.gov/autismiacc/index.cfm)

Dr. Hyman: There’s a tremendous need for research, as well, in terms of which therapies are most effective. The data to date provide the most support for behaviorally based interventions. Many families will talk about the intervention that was packaged by Dr. Lovaas, where he used principles of reinforcement to teach very young children with autism specific skills that would allow them
to be integrated into classrooms. Since he published this work in the 1980s, there have been many, many iterations of how to provide behaviorally based treatments in more natural environments to address language, to address other behaviors. And really, these behaviorally based approaches to intervention across the age span are the basis of how we educate children with disabilities and how, if you expand it in a more global framework, how we all learn.

One of the challenging things for pediatricians to do when children succumb to other situations, whether it’s trauma or other illnesses, and one of the limiting factors with autism research is the availability of brain material for basic scientists to study. There is a brain bank that is actively soliciting brains from people with autism and family members of varying ages. This is very, very precious research material. It’s precious because of the emotional impact on families, but it’s precious because it’s so rare. Despite the fabulous advances we’re making in neuroimaging, genetics, and other types of noninvasive technology, there’s really no substitute in some research for actual material.

**Dr. Rice:** Another point I would like to make is in terms of the importance of autism. The CDC and AAP put out a joint statement, called the *Autism Alarm*, indicating that, particularly from CDC’s perspective, the autism spectrum disorders are conditions of urgent public health concern, but remembering when we think of autism, the acronym ALARM is very helpful in terms of pediatric practice. Remembering that autism is prevalent, for *A*; *L*, we need to listen to parents; *A*, we need to act early; *R*, we need to refer when there’s any concern; and *M*, we need to monitor that after the referral, things don’t end. As the medical home provider, we have many years of working with the family to follow up on the child’s developmental needs and to help guide them on the next step.

**Dr. Hyman:** We’ve come to the end of our program. I would like to thank the American Academy of Pediatrics for putting together this very stimulating discussion, and I’d like to thank my colleagues, Dr. Catherine Rice and Dr. Simon Baron-Cohen, for participating.

**Narration Close**
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