AUTISM Advocate

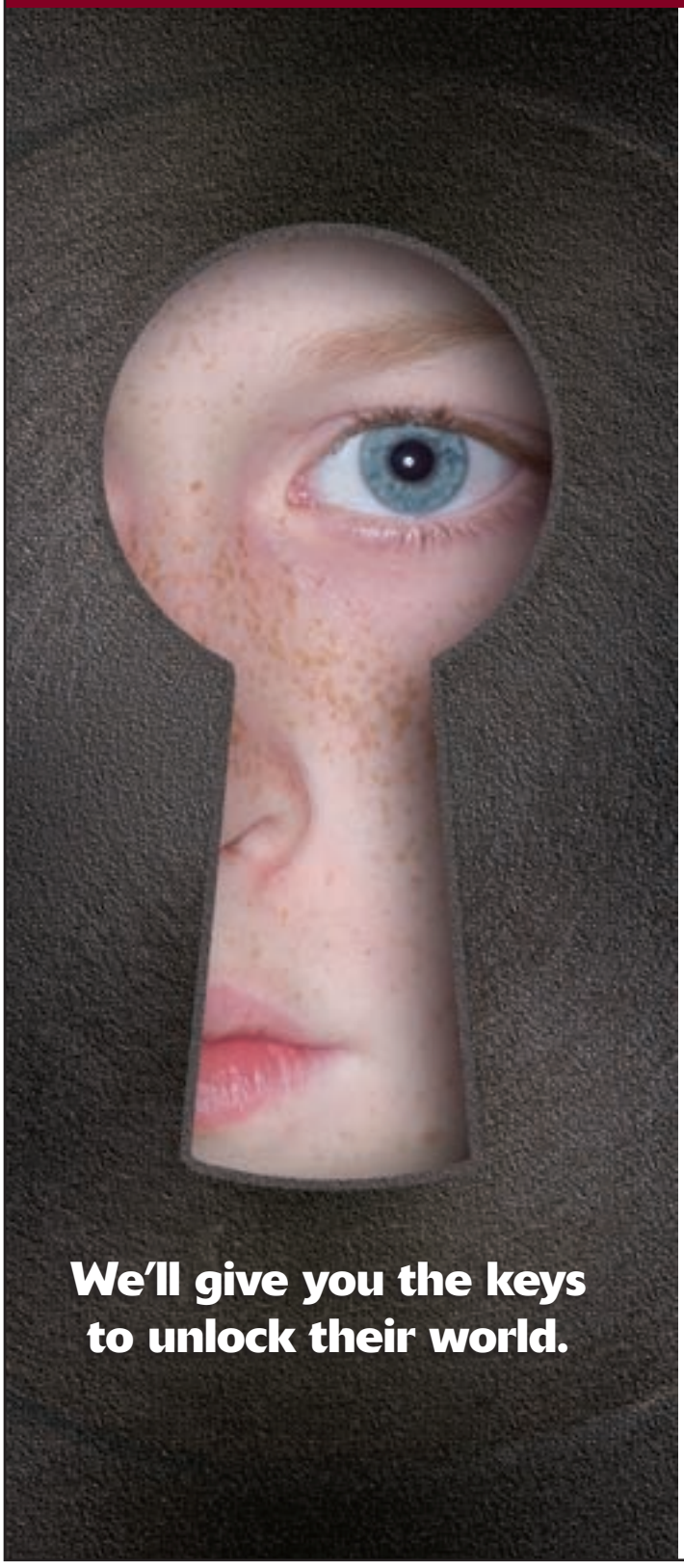
FIFTH EDITION 2006, Volume 45 № 5

Environmental Health and Autism

IN THIS ISSUE:

ASA™ Autism Society of America

Autism does not have to be a life sentence



You're not about to give up on your child.

Neither Are We.

Since 1983, the **Autism Treatment Center of America™** has provided innovative training programs for parents and professionals caring for children challenged by Autism Spectrum Disorders and related developmental difficulties.

- **Practical Tools**
- **Powerful Results**
- **Limitless Hope**

Help your child improve in all areas of learning, development, communication and skill acquisition.

Join us for our internationally-acclaimed Son-Rise Program® Start-Up, a comprehensive weeklong training program for parents and professionals.

We don't put limits on the possibilities for your child.

Free 25-Minute Initial
Call 877-766-7473

Autism
TREATMENT CENTER OF AMERICA™

HOME OF THE SON-RISE PROGRAM® SINCE 1983

2080 South Undermountain Road
Sheffield, MA 01257-9643 USA
Telephone: 877-766-7473 • E-mail: sonrise@option.org

www.autismtreatment.com

CONTENTS

December 2006

page 18 SPOTLIGHT

TIME TO GET A GRIP

BY MARTHA R. HERBERT, M.D., PH.D.

Does an environmental role in autism make sense? How do we decide? And if environment *is* involved in autism, what do we do about it?

These are challenging questions. Because our available information is complicated in many ways, each of us answers these questions based on our own judgment and deeply held worldviews.

FEATURES

An Interview with Dr. Tom Insel, NIMH Director
"We can't wait. We have to find out about which treatments will work for our children."
By Bleu Blakslee
PAGE 11

Autism's New Paradigm: Seeking Answers to Environmental Threats
By Michael Lerner, Ph.D.
PAGE 13

COVER PHOTO: © WILL TERRY

ARTICLES

Biomedical Factors in Autism

For more articles, please visit www.autism-society.org/advocate.

Treatments for Autism

Autism: First Person Perspective

DEPARTMENTS

MESSAGE FROM THE ASA BOARD CHAIR

In Memoriam

The Autism Society of America (ASA) announces with profound sympathy the death of our founder, Bernard Rimland, Ph.D. Bernie Rimland was among the first to realize the importance of combining a focus on medical interventions with treatments, supports and services. There is not one parent or professional who has not been impacted by the knowledge, dreams and thinking of Bernie.

A pioneer in the area of autism diagnosis and treatment, Bernie transformed the prevailing pessimistic view of autism in the medical and scientific community and built the largest parent support organization in the United States. Along the way, he inspired hundreds of thousands of parents, advocates and professionals to treat individuals with autism with respect, dignity and care.

His 1964 book, *Infantile Autism: The Syndrome and its Implications for a Neural Theory of Behavior,* was responsible for challenging and changing the long-held belief that autism was an emotional disorder caused by poor mothering. Autism is now recognized as a biomedical disorder. Bernie devoted himself tirelessly to conducting and disseminating the results of research on methods of diagnosing and treating the full spectrum of autism. These treatment modalities,

> "There is not one parent or professional who has not been impacted by the knowledge, dreams and thinking of Bernie."

once considered radical, are now gaining wide acceptance as the news spreads about formerly autistic children who have been reclassified as normal.

Bernie's determination was spawned by his own son's diagnosis of autism, at age two, in 1958. He was a hero to the autism community and his legacy will live on through the work of the Autism Research Institute, the Autism Society of America and the good work of others. This special edition of the *Autism Advocate* is dedicated in Bernie Rimland's memory.

Cathy Pratt, P.h.D.

AUTISM Advocate
ASA's Premier Magazine on Autism Spectrum Disorders

PUBLISHER
Lee Grossman, ASA President and CEO

MANAGING EDITOR
Kate Ranta

DESIGN
n2design, Inc.

ADVERTISING SALES
Potomac Media

ASA DIRECTOR OF COMMUNICATIONS
Marguerite Kirst Colston

The *Autism Advocate* is published five times a year. To receive the publication, please join the Autism Society of America. For more information, please visit www.autism-society.org. To contact the editor, please email editor@autism-society.org.

If you are interested in advertising in the *Autism Advocate*, please contact Reem Nourallah at 202-333-8622 or Potompub@aol.com.

All other inquiries should be directed to:
Autism Society of America
7910 Woodmont Avenue, Suite 300
Bethesda, MD 20814
Toll free: 1-800-3AUTISM | Fax: 301-657-0869
www.autism-society.org

Now Available! September 2006 Edition

—

Newly Revised and Updated

RECOVERING AUTISTIC CHILDREN

How-to-do-it information from parents and physicians

Edited by Stephen M. Edelson, Ph.D. and Bernard Rimland, Ph.D.
Autism Research Institute

"More progress has been made—and more autistic children have recovered—in the past three years than in the past three decades."

The Editors

Recovering Autistic Children is the extensively updated and enlarged revision of *Treating Autistic Children*, which was published in 2003.

Almost all of the 31 parent reports have been updated and 83 pages of new information have been added. You'll find up-to-the-minute information from ARI's acclaimed Defeat Autism Now! (DAN!) Project and new sections including Hyperbaric Oxygen Treatment (HBOT); clinical use of Methyl B12; Specific Carbohydrate Diet; Low-Dose Naltrexone; Chelation; Medical Marijuana to control aggression; and much more!

Thousands of autistic children have recovered and are recovering, based on the sound information in this book. (Seeing is believing! Go to www.Autism-RecoveredChildren.org.)

Order your copy today!

Paperback, 2006, 468 pages, $22.00

AUTISM RESEARCH INSTITUTE: RESEARCH THAT MAKES A DIFFERENCE — SINCE 1967

4182 Adams Avenue, San Diego, CA 92116 • www.AutismResearchInstitute.com

---

AUTISM RESEARCH INSTITUTE

Mail or fax to: 4182 Adams Avenue, San Diego, CA 92116 • Fax (619) 563-6840

The Institute is supported by donations from concerned individuals and organizations. Donations are needed and are tax deductible. Federal Exempt Designation: 501(c)(3). Federal I.D. No. 95-254-8452

Name _____

Address _____

City_____State_____ Zip_____ Country_____

Phone_____ Fax_____ Email_____

___ Check enclosed ___Bill my credit card

__VISA __MasterCard __Discover

Card #_____ Exp. Date. _____

Signature _____

Recovering Autistic Children *($22)* $_____

California residents add $1.71 $_____

shipping/handling *(U.S. $2; overseas $5)* $_____

Check here for publication list___ no charge

DONATION..... $_____

TOTAL ENCLOSED: $_____

TO ORDER ONLINE:
visit www.AutismResearchInstitute.com

MESSAGE FROM ASA PRE

Lee Grossman

On behalf of the Autism Society of America (ASA), its board of directors, our tens of thousands of members and supporters, and our network of almost 200 chapters, I wish to thank the contributors to this special issue of the *Autism Advocate,* "Environmental Health and Autism." Representing a seminal treatment of this topic, this special issue contains the most up-to-date research and opinions from a variety of thought leaders that consider and challenge the many long-held concepts on the causes and treatments for autism spectrum disorder (ASD). This special issue is part of a larger project at ASA, which boldly proposes a new paradigm in how we deal with ASD issues. The collective wisdom of those contributing to this journal supports new theories, while at the same time factoring important lessons learned and showing the utmost respect and concern for all those affected by ASD.

Many have asked why ASA is becoming involved with environmental health and autism now, but when we look back at our history, our organization has always been concerned with this issue. Our founder, Dr. Bernard Rimland, has been on the forefront of this for decades, and we have held conferences and produced numerous articles in our publications on this subject. Moreover, our public policy initiatives have been consistent and vocal in the need for further and expanded research.

This special issue is part of a larger project at ASA, which boldly proposes a new paradigm in how we deal with ASD issues.

Nonetheless, we have witnessed over the past few years that the effects of environmental toxins have become much more visible, and thus the debate more global. But within that discussion, there has been much controversy, defensiveness and divisiveness. The effects of environmental factors and toxicity have been well established and accepted in numerous other disabling conditions, and have become a uniting element in many condition-specific communities. With ASD, it has had, to a large degree, an opposite effect in which the differing parties have reached entrenched positions, with polarizing effects.

In undertaking our Environmental Health Initiative, ASA believes it is time to structure a dialogue on the subject that looks at the issue anew. Our objective is to look at the reality, and from that begin to build an objective and scientific basis to this new paradigm of thinking about ASD.

Our premise was based on the following tenet:

ASD is thought to be a genetically based, neurological and lifelong condition that has reached alarming levels of incidence. Recent studies have put the incidence at as many as 1 in 166 births. This dramatic, significant and unabated rise in individuals diagnosed with ASD is creating an economic burden on society and producing a national heath crisis. Assuming the basis of ASD is genetic, what has happened recently that would so profoundly affect these large numbers to occur? Reasonable attention has been focused on the possibility of neurotoxicants and/or environmental health concerns as culprits in damaging the gene construct and "triggering" the symptoms known as ASD.

SIDENT & CEO

Major public policy considerations weigh heavily on this. If we are to accept the basic definition of autism as a genetically based neurological condition, then it must be approached as a medical condition. Accepting autism as a medical condition will have enormous positive effects on public policy, as we will no longer be subjected to the archaic and typically limiting policies that are imposed through the systems of services of developmental disabilities and/or mental health. As a medical condition, those with ASD and their families will be able to receive services and treatments similar to those of other medical problems, with insurance and appropriate coverage to handle their specific needs.

Through our work on the Environmental Health Advisory Board and the Environmental Health Initiative, we hope to bring credibility to this subject where it will be considered and accepted by the "mainstream" medical community. Some excellent work and science notwithstanding, the medical community in 2006 is not typically supportive of the theories of environmental issues contributing to autism, much less the basic and overwhelming belief held by ASA that autism is a treatable condition. It is time for this opinion to change—and this will only be accomplished through thoughtful and meaningful science that creates an objective body of work that is a compelling, without bias and overwhelmingly supportive of the medical, whole body condition of autism.

ASD has primarily been treated through educational, behavioral and psychosocial modalities. It has been through the dedication and expertise of multitudes of professionals such as teachers, psychologists, behavioralists, occupational therapists, speech pathologists, service providers, recreational aides, etc. that our children and adults on the spectrum have improved. Their hard work and passion to help those with ASD will continue to be a critical and essential part of the service, treatment and intervention programs necessary to better the lives of those with ASD. The amount of applied research produced through these professionals per year is equal to, if not greater than, the total amount of biomedical research on autism. This has been accomplished with minimal and limited funding, and little to no fanfare. I will always be grateful to them for the impact they have had on my son's life and their contributions to the autism community.

With that said, perhaps the most important reason to pursue the medical paradigm of environmental effects on autism is that it may be the most significant way to achieve medical treatments for those with ASD. If a person is not treated for a serious gastric or digestive tract disorder, suffers from severe allergies or is unable to properly process common and/or toxic sequelae, it will be difficult for them to adjust, adapt and learn. If we are to effectively treat a person with ASD medically for some coexisting or underlying medical problem, it will allow the complementary approaches of educational, behavioral and psychosocial interventions to be that much more successful.

Autism is treatable and, in many cases, is associated with a coexisting chronic medical condition. Research must be conducted towards identifying the genetic predisposition of those on the autism spectrum, and how environmental exposures contribute to creating the "perfect storm" in producing the symptoms we describe and diagnose as ASD.

We are on the cusp of a new and better age for autism. I hope that we soon will identify the underlying factors that cause a person to have the symptoms of ASD. As it is now, there is a very low percentage of children that are losing the diagnosis through effective therapies. This must become the norm for the majority that are diagnosed with ASD. It must become an accepted part of mainstream medical thought to predict, prevent and/or reverse the symptoms of ASD, in order to maximize the truest potential for the majority of those living with ASD. We will then truly improve the lives of all affected by autism.

Lee Grossman
President and CEO, ASA

FROM ASA'S ENVIRONMENTAL

CO-CHAIRS MARTHA HERBERT, M.D., PH.D. AND DAVID HUMPHREY

Is autism affected by our environment? A growing body of speculation and information suggests a connection.

In 2005, Dr. Carol Berkowitz, then president of the American Academy of Pediatrics, made a striking statement: "I think there's a real concern that there's been a change in our environment. An exposure to some toxins, chemicals, environmental factors—either when a mother is pregnant or after the delivery of the child—that has led to autism."

This same concern is shared by the American public: in a recent MSNBC poll, more than 80 percent of those surveyed placed the blame for autism on environmental factors impacting individuals who are genetically vulnerable.
When we acknowledge a potential role for the environment in contributing to or causing autism, we also acknowledge the possibility that autism may be *predictable, preventable and reversible (treatable).* Making this possibility a reality will then need to become a top priority, and this will have a far-reaching and profound impact on future research as well as medical, educational and other public policies regarding autism.

In February 2006, the Autism Society of America (ASA) formed an Environmental Health Advisory Board (EHAB) to explore the connection between the environment and autism. Board members were chosen based on academic and professional backgrounds in environmental health and in autism, and represent some of the best minds in these areas.

EHAB's mission is "to improve the lives of individuals with autism by fostering an understanding of environmental contributors to the onset and severity of this condition." Toward this end, EHAB decided that it was important to compile current and reliable information regarding the possible link between autism and environment. Leading experts from a wide range of disciplines related to environmental health and autism were asked to contribute to this effort. The result is this special edition of the *Autism Advocate.*

We want to thank ASA for providing a forum for this important discussion. We also want to thank our committee members (listed below) for their willingness to take on this ambitious project; the John Merck Fund for their generous grant that helped fund this special issue of the *Autism Advocate;* our contributors for sharing their expertise and insights; and a special thanks to our editors on this project, A. K. Blake, Kulani Mahikoa and Kate Ranta.

Environmental Health Advisory Board Members

- **Joan Cranmer, Ph.D.,** is a professor of pediatrics and pharmacology/toxicology at the University of Arkansas for Medical Sciences, and editor-in-chief of *NeuroToxicology.* In 1996, she served as an advisor to the White House Committee on the Environment and Children. She received the Joseph P. Kennedy Research Award for outstanding contributions to pediatric research for publishing in *Science* the first research paper on "behavioral teratology." She received her Ph.D. from the University of Minnesota, and completed her post-doctoral work at the University of Virginia at Charlottesville. Her research interests include infant and child neurotoxicity studies, children's environmental health and developmental neurotoxicology. Dr. Cranmer organizes and chairs an annual international neurotoxicology conference which has a strong focus on advances in autism spectrum disorders.

- **Lee Grossman** is president and chief executive officer of the Autism Society of America. The parent of a 19-year-old son with autism, he has been involved with ASA since 1992. He is a past president of the Autism Society of Hawaii, and has been on ASA's Board of Directors since 1995. He also was appointed in 2001 to serve on the Interagency Autism Coordinating Committee (IACC), which is tasked with coordinating autism efforts among all of the federal agencies.

- **Ruth Elaine Hane,** First Vice Chair, ASA Board of Directors, Nominating Committee, Chair, Strategic Planning Committee, holds a B.S. in human ecology from the University of Minnesota. Ruth Elaine was diagnosed with high functioning autism in 1995.

- **Robert Hendren, D.O.,** is professor of psychiatry, Tsakopolous-Vismara chair and executive director of the M.I.N.D (medical investigation of neurodevelopmental disorders) Institute, chief of child and adolescent psychiatry at the University of California, Davis, and president-elect (president 2007-2009) of the American Academy of Child and Adolescent Psychiatry. Dr. Hendren took his residency in general psychiatry at the Mayo Graduate School of Medicine in Rochester, Minn., and his child and adolescent psychiatry fellowship at the Yale Child Study Center. His primary areas of research and publication interests are translational clinical

HEALTH ADVISORY BOARD

pharmacology and nutritional trials using biomarkers (MRI, measures of inflammation, oxidative stress, immune function and pharmacogenomics) in neurodevelopmental disorders.

- **Martha Herbert, M.D., Ph.D.,** is an assistant professor of neurology at Harvard Medical School, and a pediatric neurologist at the Massachusetts General Hospital in Boston and Cambridge Health Alliance Center for Child and Adolescent Development. She received her medical degree from Columbia University College of Physicians and Surgeons, did her pediatric training at Cornell University Medical Center in New York City and her neurology training at the Massachusetts General Hospital. Prior to her medical training, she earned a Ph.D. in the History of Consciousness at the University of California, Santa Cruz. She studies brain size and brain coordination problems in autism, how body problems affect the brain and how researchers can measure changes in brain function that can result from treatment interventions. She brings to her current work a long history of interdisciplinary and organizational research and experience.

- **David Humphrey** is a board member of the Northwest Autism Foundation, the Autism Treatment Network (ATN), the Autism Society of America (ASA) and the Autism Research Institute (ARI). He is also the president of Kirkman Group, Inc., a pharmaceutical company in Portland, Ore. For the past five years, Mr. Humphrey has devoted much of his time to the research and study of autism. He is a successful entrepreneur who has founded several companies in Oregon and Hawaii. One of his companies was named for four consecutive years to *Inc*. magazine's prestigious list of "500 Fastest Growing Companies in the Nation." *Oregon Business Magazine* also named Kirkman Group, Inc. as one of the "Top 100 Companies to Work for in Oregon."

- **Jennifer LeFever** is Director of Information and Referral/ Customer Service for the Autism Society of America. She has worked in the developmental disabilities field since 1992. Her work experience ranges from direct support for individuals with disabilities to systems advocacy and public policy work. Jennifer has a degree in Rehabilitation Services and Education from Penn State University.

- **Michael Merzenich, Ph.D.,** is Francis A. Sooy Chair of Otolaryngology in the Keck Center for Integrative Neurosciences at the University of California at San Francisco. He is the founder of Scientific Learning Corporation and Neuroscience Solutions Corporation, which develop therapeutic programs for the neurologically and psychiatrically impaired. With his wife Diane, he established the Merzenich Chair in Education at the University of Portland. His chief area of interest is the "brain plasticity" underlying the development of skills and abilities through experience and learning. He is a medical inventor who has been awarded more than 50 patents, and his group developed the first models of a commercial (Clarion) cochlear implant.

- **Elise Miller, M.Ed.,** is founder and executive director of the National Institute for Children's Environmental Health, and in that role, serves as the national coordinator for the Collaborative on Health and the Environment's Learning and Developmental Disabilities Initiative (www.iceh.org/LDDI.html). She also serves on the Children's Environmental Health Network national board of directors and the advisory boards of several other national organizations. In addition, she completed a fellowship at the Fetzer Institute, based in Kalamazoo, Mich., for her work on sustainable development and environmental health. She received her Master of Education degree from Harvard and her Bachelor of Arts degree from Dartmouth College.

- **Isaac Pessah, Ph.D.,** is professor of toxicology and director of the Center for Children's Environmental Health Sciences in the Department of Molecular Biosciences at the School of Veterinary Medicine, University of California, Davis. He completed his undergraduate training at Cornell University, and received his Ph.D. in pharmacology and toxicology from the University of Maryland.

- **Bernard Rimland, Ph.D.,** was director of the Autism Research Institute (ARI) in San Diego, Calif., and founder of the Autism Society of America (ASA). He was also the director of ARI's Defeat Autism Now! (DAN!) project, coauthor (with Stephen M. Edelson) of *Recovering Autistic Children,* and editor of the *Autism Research Review International.* In 1964, he won the Century Prize for Distinguished Contribution to Psychology for his first book, *Infantile Autism,* which revolutionized the field of autism research and treatment. His son, Mark Rimland, who has autism, is an internationally recognized artist.

- **Stephen Shore** was diagnosed as a child with "atypical development with strong autistic tendencies," was nonverbal until four, and was recommended for institutionalization. He is now completing a special education doctorate at Boston University focusing on helping people with autism develop their capacities to the fullest extent possible. In addition to authoring three books, presenting and consulting internationally, he serves on the board of the Autism Society of America and several other autism spectrum-related organizations.

As vital as they are, love and best intentions aren't enough to secure the future of a special needs child. She needs the specialized knowledge of a Special Needs Alliance lawyer – someone particularly skilled at the hide-and-seek of disability laws and public benefits preservation. Estate planning, too – to ensure everyone in your family gets the financial hand-me-downs they need. Contact your nearest Special Needs Alliance member today: **877-572-8472** or visit **www.specialneedsalliance.com**.

Special Needs Alliance

Special needs require special lawyers.

AN INTERVIEW WITH DR. TOM INSEL, DIRECTOR OF THE NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)

"We can't wait. *We have to find out about which treatments will work for our children."*

BY BLEU BLAKSLEE

Q: Where is the federal government in its commitment to finding treatments for autism?

A: Autism is one of those disorders for which the federal government has a plan put together through five of the institutes from the National Institutes of Health (NIH), the Center for Disease Control and Prevention (CDC), the Department of Education, and a few of the other agencies, most of which are in the Department of Health and Human Services. That plan is organized around the Interagency Autism Coordinating Committee (IACC), which meets twice a year and has a number of public members. It is really a project in a sense to make sure that we are making progress, and to make sure that we have our eyes on the prize, and that we have a plan to move forward on very specific initiatives for autism that are coordinated across all of these different agencies.

So in [NIH's] case, what we did was develop a "roadmap," which is essentially a matrix of anticipated efforts over the next 10 years—some of them are short term, some are long term, some are relatively modest and straightforward, and some are a real reach and will be high risk and difficult to get to. But, we have laid these out in an action table, if you will, and it is a chance to look at questions like: What do we need to do, what do we need to do first, and what are the ultimate goals? Where do we want to be in 10 years, and what are the things we really need to keep our sights on? And to get to those points, what are the intermediate steps we are going to have to make? Our roadmap is available on the Internet and also on the NIMH Web site (www.nimh.nih.gov).

Q: With everything going on in the autism community, is this the right time to focus on treatment?

A: Good question. Are we ready? Should we even do this before we know the basic biology of this illness? And the answer is: We have to. We can't wait. We have to find out about which treatments will work for which children. Among the treatments that we have now, we don't have a cure and that is very clear. And we will not have a cure, most likely, until we know a lot more about this disease or diseases, because autism may be several disorders with one name. But in the meantime, we have to move ahead with a set of treatments that will target specific aspects of this disorder.

So it may not be a single treatment for the whole thing, but there ought to be treatments that will at least make it easier for children to be able to be mainstreamed in school, for children to be able to cooperate with behavioral therapy and to be able to use it. There ought to be treatments that help kids to at least get a leg up on this disorder and to help families, which is really just as important, and that is part of what we are looking at right now. So I think this kind of a focus on treatment is a great idea, and we need to get to a point where we have some things that we know have an evidence base that we can tell people should work most of the time. And what we ultimately need to know is individual pattern of response—which treatment for which child—and that we don't know yet.

Q: What is reasonable to expect in the next three to five years?

A: Right, so what can we actually get done? The hard thing about research is you don't know exactly where it is going to take you, and you don't know exactly how long it is going to take you to get there. It is usually much longer than you expect, and there are usually lots of side trails before you find the main road. We really have to find our way. A lot of that, unfortunately, is going to be trial and error, and so it is hard to put a timeframe on it. It is hard to say where we will be in three years, where we will be in five years. I think the better thing to say is where will we have the most traction? And the traction, clearly, to some extent, is in genetics. The traction is in some of these early treatment trials like the RUPP [research units on pediatric psychopharmacology] network that is beginning to give us some insight about some valuable treatments for what you could call secondary symptoms. They don't go for the core symptoms, but they do help children.

There is traction, I think too, in trying to understand the disorder—trying to get a handle on what the subtypes and key features of the disease are that need to be emphasized. I think that is where we will be over the next three to five years. The genetics will help us a lot because that is one place that is moving so quickly, but that is also going to be problematic; for us to get the genetics right, we have to make sure we understand the different subtypes of this syndrome, because if it is several disorders, it may have several different genetic components.

Q: Can you talk a little bit about your perspective on whether there is value in a public-private partnership?

A: Good question. A lot of research in the past has often been driven by one of the NIH institutes with a real partnership with an academic health center. This is going to go differently, I think. This is really going to be a case in which we need three partners. We need families, we need clinicians who are on the front line,

and we need the scientists. And that is a little bit different than the way it has been done before.

I think this is a case in which the parents really have a lot to bring to the table and, in many cases, they really are the experts in specific aspects of this disorder, at least for their child. They have lived with this. They have struggled with it and they have figured out what works and, sometimes, what doesn't work. The clinicians also increasingly can bring a lot of important insight. We are still at a stage where we need to have careful clinical descriptions of the components of this, how they match up, what are the subtypes, and how many disorders do we actually have. And I think getting clinicians more involved and getting them to think of this more as a multisystem disorder—bringing in clinicians that can think about the gut symptoms, and the sleep problems and problems around the immune function—all of that will be really important as we try to pin down what we call the phenotype of this disorder.

And then the third piece will be the researchers. The researchers have been chipping away at this all along. I think the big difference, as we go forward, is we need to bring in other kinds of scientists. We need to bring in other people who haven't been in the autism field, but the people who have made major findings in related fields—in developmental neurobiology, sometimes in genetic illnesses where they have found other genes in developmental disorders—people who have really thought very carefully about such things as epigenetics and immune function and a whole bunch of other areas which, so far, have not been within the domain of autism research. So part of what we are talking about here is not just a partnership, but enlarging some of the partners in some very strategic ways.

Q: What is your general assessment of where we are in treating kids with autism around the U.S. and about the gap that exists?

A: There is quite a bit of information regarding the quality of treatment that is available, and most of the news isn't very good. We know that in autism, maybe even more than other disorders, early is better. The sooner you can intervene, the better the outcome. That is very clear. The average age at which children are diagnosed has unfortunately been after the most sensitive time for intervening, so you often find, for instance, in one study that was published a few years ago using a Medicaid population in Philadelphia as I recall, the average age was somewhere around six, maybe even a little bit later. For African American children, it was a year and a half beyond that. So we have health disparities.

The children of minority and poor parents are not getting diagnosed as early. And even the more general population of kids who may not belong to one of these underserved populations is still getting diagnosed far too late. We need to focus on early detection/early intervention. That is going to make a big difference for at least 25% of those children who have this disorder.

Q: Other comments?

A: There is a balance here. You always have to find the balance between providing treatments that we know about and improving treatments, and going after the big research questions. So much…[of] this is comparable with respect to 50 years ago, facing the polio epidemic. Then, you could have imagined a very similar discussion where one group of people would have said, "You know, what we really need is to figure out how to make a smaller, better, cheaper iron lung and make sure that every child [will] have access to those iron lungs." That is certainly commendable and important, but if we had stopped there, we would have never had a vaccine, and we would have had hundreds and thousands of children today with iron lungs. So we need to find that balance.

On the one hand, [that balance requires] making sure you have treatments that you can put out now for families and children who needed them yesterday and making sure they are available and making sure they are evidence-based and you have tested them rigorously so that you are not doing more harm than good; but at the same time, you have to keep your eyes on the prize. Where is the opportunity for a cure? Where is the opportunity to pre-empt this whole thing? That is the vaccine for polio. That is the question that you can't duck at a time like this. You have to keep both things in mind: doing what you need for today, but also thinking long term: What do you need for tomorrow?

> "We need to focus on early detection/early intervention. That is going to make a big difference for at least 25% of those children who have this disorder."

INTERVIEWER
Bleu Blakslee is the development coordinator for the Autism Treatment Network and a freelance development consultant.

Autism's New Paradigm:
Seeking Answers to Environmental Threats

BY MICHAEL LERNER, PH.D.

The new paradigm of autism proposes the following: autism is not a strictly inherited disease; environmental factors contribute to its incidence; and dietary interventions, detoxification strategies and other treatments may contribute to amelioration or even recovery.

We know that the scientific and public response to the new paradigm of autism has been mixed. There are dedicated scientists and clinicians who continue to insist that environment plays no role in autism. They believe, in principle, that dietary modifications and other proposed medical treatments cannot contribute to amelioration or cure.

On the other side are dedicated scientists, clinicians and parents who are equally certain that the new paradigm of autism is true with respect to etiology, treatment and prevention.

In the middle is a wide spectrum of people who are open to the new paradigm of autism hypothesis, but are not certain whether it is true or to what extent it is true. This present majority of scientists, clinicians and families want to see the theory subjected to scientific evaluation that is truly open to the evidence and that addresses the theory with the great urgency it deserves.

I have dedicated much of the past 30 years to evaluating complementary and alternative medical (CAM) approaches to health. I have specialized for the past 20 years in studying CAM therapies for cancer. Before that I spent a decade studying CAM therapies for children with learning and behavior disorders. So, I address this issue of CAM therapies for autism with extensive knowledge about these approaches.

I am equally engaged with the community of scientists and health professionals exploring the revolution in environmental health sciences, which is looking carefully at the impact of the

environment on almost 200 different diseases, disorders and conditions. Understanding the plausibility of the new paradigm of autism requires understanding the revolution in environmental health sciences.

It makes the most sense to start this discussion of the new paradigm of autism by looking through the broad lens of the revolution in environmental health sciences and then coming back to the clinical and research issues.

The Ecological View of Health and the Environmental Health Science Revolution

I wrote an essay a decade ago called "The Age of Extinctions and the Emerging Environmental Health Movement." I said that scientists know we are living in the sixth great age of extinctions in the history of the earth. We are driving biodiversity back 65 million years to its lowest level of vitality since the end of the age of dinosaurs. There are five major causes of this new age of extinctions: climate change, the depletion of the ozone layer, toxic chemicals, habitat destruction and invasive species.

"This means that personal health and environmental health are inseparably connected. The environment is not only outside us; it is inside us."

The first three causes of this "age of extinctions" all reflect the reality that we live at the end of the hydrocarbon century in which we have learned how to pump fossilized sunlight and stardust – carbon resources and heavy metals – from their safe resting place under the earth's mantle and turn them into toxic chemicals and gasses that are changing the earth's atmosphere and building up in our bodies.

There are many other threats to human and environmental health: poverty, infectious diseases, nuclear radiation, electromagnetic fields, and the new threats of biotechnology and nanotechnology. All of these factors interact in an infinitely complex "soup" in which our genetic make-up is bathed from conception to death. This means that personal health and environmental health are inseparably connected. The environment is not only outside us; it is inside us.

So, autism is far from the only disease that is or appears to be increasing as a result of environmental change. Ted Schettler, M.D. science director, Science and Environmental Health Network, has argued that many of the endemic diseases of our time can best be understood as ecological diseases that are a function of the totality of the disruption of environmental and human ecosystems. Only an ecological view of health, Dr. Schettler reasons, enables us to understand, study and remedy our current condition in an appropriate and effective way.

This ecological view of health has emerged over the past two decades from what Pete Myers, Ph.D., CEO, Environmental Health Sciences, has called the revolution in environmental health sciences. This revolution has been driven in significant part by the discovery of endocrine-disrupting chemicals, which have fundamentally shifted the old paradigm of how chemicals affect our health. The old paradigm focused on large doses of chemicals and how they affected adult health. The new paradigm focuses on the powerful health impacts of some chemicals that affect fetal development at infinitely lower doses – parts per billion or trillion – at critical stages in fetal development. Following is an example of how a chemical (in this case, a drug) caused harmful effects to the children of the women who took it.

I am a DES son. My mother took di-ethyl-silbestrate, believing it would protect her from the series of miscarriages that preceded my birth. DES, it turned out, caused reproductive cancers in lab rats, a fact that the pharmaceutical industry knew while it was promoting this medicine for pregnant women. Decades later, physicians accidentally found that DES was causing reproductive cancers in the daughters of women who took this medicine. The impact on DES sons is less clear, but many of us have benign prostatitis and other conditions. DES was the first endocrine-disrupting chemical discovered by scientists. Now we know of hundreds of chemicals that disrupt the endocrine system and other key signaling systems that affect the health of the developing fetus in hundreds of different ways.

The Vaccine Controversy and the New Paradigm of Autism

Endocrine-disrupting chemicals may or may not contribute to what is apparently an epidemic of autism. Skeptics insist that what we are witnessing is simply a shift in diagnostic categories. The specific contaminant of greatest concern to thousands of parents across the country and around the world who believe in the environmental connection to autism is mercury. The claim is that the mercury in vaccines often plays a critical role in sending normally developing children into an autistic regression.

The vaccine controversy has engulfed rational dialogue about the etiology of autism in ways that many responsible

scientists do not believe serves the field best. First, there are numerous sources of environmental mercury exposure other than vaccines. Second, there are good reasons to believe that mercury is not the only environmental trigger for autism. Gluten sensitivity, for example, has also been implicated. Third, we cannot really assess any environmental contributors to autism as long as we remain in a paradigm of autism that considers the disease exclusively inherited. That is why framing the issue as an inquiry into the "new paradigm of autism" is far preferable from the perspective of both scientific understanding and the urgent need for clinical progress.

Whatever your views on the vaccine controversy, imagine that ultimately research demonstrates that vaccines have been a significant contributor to autism – a claim that leading medical authorities have vigorously denied. Even if the advocates of the vaccine hypothesis turn out to be right, this will prove only to be a start to examining the broader research and clinical need for a new paradigm of autism. The most important point is that we can address the need for a new paradigm of autism research in a much less inflammatory way by setting the vaccine hypothesis aside. Once the case for a new paradigm of autism is established, the vaccine controversy can then be addressed for what it is – one and only one of the potential contributors to the development of autism.

I personally believe that the new paradigm of autism fits the clinical facts and the theoretical conclusions being derived by the scientists and clinicians who are leading the environmental health science revolution. At the same time, I remember well the enthusiasm of parent groups at the time allergist Ben Feingold, M.D., proposed that food additives were the leading cause of attention deficit hyperactivity disorder (ADHD). I investigated these claims with some care at the time they were made three decades ago. It turned out that some cases of ADHD were triggered, if not caused, by exposure to food additives. But the real roots of the epidemic of ADHD can be found in the far more complex set of all the environmental exposures of the developing fetus and young child. Thus, the Feingold hypothesis was in many ways like the vaccine hypothesis. It was a partial truth, but the debate between true believers in the Feingold Diet and its most vociferous opponents in many ways obscured the more important truth of the new paradigm of learning and developmental disabilities that has emerged over subsequent years.

My own perspective is that some of the claims being made with respect to both environmental causation and CAM medical treatment of autism will turn out to be excessive. I have talked to many parents of autistic children who made sincere and extended efforts to help their children with these CAM medical treatments to no avail whatsoever, and at great financial and personal cost. I have also seen convincing documentation of children who have greatly improved, and in some instances recovered, using these CAM therapies.

The Clinical, Research and Policy Imperatives for Progress in Autism Research and Treatment

The real research and clinical issues facing those in the autism field are that we urgently need to 1) document the best cases of clear-cut recovery, or major amelioration, of autism associated with *all* treatments, including CAM medical treatments, purely behavioral treatments and combinations of the two; 2) rigorously explore the theoretical new paradigm of autism to account for what appears to be happening both in causation and in occasional successful CAM medical treatment; 3) learn how to identify those children for whom expensive, arduous CAM medical treatments are most likely to be successful; 4) address the question of how to make medical as well as behavioral treatments available to all who seek them out; 5) educate parents about which treatments, both medical and behavioral, to undertake with their children; and 6) explore which policies we should support that make effective diagnosis and treatment available, and that prevent as many future cases of autism as possible.

These are the research, clinical and policy issues in autism. Let us now turn to the broader context of this debate in both environmental health and integrative medicine. For the past five years, I have been deeply engaged in the development of the Collaborative on Health and the Environment. The collaborative is an international partnership of individuals and organizations seeking to raise the level of public and professional dialogue on the impact of the environment on human health. The collaborative now has over 2,250 organizational and individual partners in 47 states and 32 countries, including a "who's who" of leading environmental health scientists, patient advocates, health professionals and other concerned citizens.

The Autism Society of America is, I am pleased to say, one of the lead members of one of the most effective working groups in the collaborative, known as the Learning and Developmental Disabilities Initiative (LDDI). The collaborative has other working groups on science, integrative health, cancer, asthma, infertility and pregnancy compromise, and Parkinson's disease.

What has emerged from the work of the collaborative over the past five years is that the debate over the new paradigm in autism research and treatment has almost exact parallels to many other disease groups, such as breast cancer, Parkinson's disease, and infertility and pregnancy compromise. In some areas, such as asthma, the role of environmental toxins is well defined. But in many diseases, such as breast cancer, Parkinson's disease, and infertility and pregnancy compromise, the new science indicates an infinitely complex interaction among genetic inheritance, gene expression as modified by fetal exposure to endocrine-disrupting chemicals, diet, stress, income disparities, ethnicity, exercise and numerous other factors.

What seems to be the case in Parkinson's disease and autism, to narrow our inquiry further, is that we are not dealing with single diseases but rather with families of disease clustered under diagnostic categories. What seems to be true in both conditions is that a wide range of different environmental "hits" at different points during human development interact with all the other factors named above and finally converge in one or another common pathway and emerge as a syndrome that is given a single label.

What this means in reality is that the search for a single unitary "cause" of these diseases will ultimately prove fruitless. We will rarely find a single chemical exposure, be it pesticides for Parkinson's disease or mercury for autism, that operates in a genetic or environmental vacuum. It may turn out to be that pesticides are a more significant contributor to Parkinson's disease than other exposures, or that mercury is a significant contributor for some subset of autism cases. But these and many other diseases will ultimately have to be explored in light of the environmental health sciences revolution and the emerging paradigm of ecological health, in which the full complexity of all environmental and heritable factors drives our understanding of the clinical, research and policy issues.

Environmental Awareness

Does this lead us to a sense of hopelessness about making progress on autism, Parkinson's disease or the hundreds of other common diseases of our time? Not at all. It leads us to an awareness that if we are facing an epidemic of ecological diseases, we must craft responses at the personal, public health and ecological levels.

At a personal level, the strategy for lifelong health for ourselves and our families is to reduce potentially harmful exposures and increase personal resources for resilience. The approaches for achieving this are well known: a healthy diet, exercise, stress reduction, reduction of harmful exposures and the like. At the public health level, the same is true for our communities – local, regional and national. At the ecological level, the same is true for our ecosystems – personal, regional and global. At each level, there are, of course, limits to what we can accomplish. It is ultimately impossible to have a healthy and thriving human community on a sick planet. But transforming human health in positive directions must happen at every level. People who understand health promotion and disease prevention at a personal and family level are more likely to care about creating healthy local communities. People who care about healthy communities want healthy states, eco-regions and countries.

I saw a bumper sticker as I was driving home one day that summed up this truth in six words: "One People. One Planet. One Future." The new paradigm of autism is not just a strategy for parents of autistic children. If mercury proves to be a significant contributor to autism, then the incidence of autism in the United States will turn out to be inseparable from the coal power plants that are proliferating in China. Advocates for autistic children are right to focus on treatment and prevention for children and families right now. But we also should recognize that the epidemic of autism affecting our families is part of a much bigger pattern of all the environmentally connected diseases that are affecting us all, not only in America, but around the world.

If these issues interest you, we welcome you in the national and international community of dialogue about the environmental health science revolution and the health of our families and communities. The Collaborative on Health and the Environment is free to join and we will never use your name without your explicit permission. You can check out the collaborative at www.healthandenvironment.org. You can make your voice heard not only for your own family, but for the whole human family.

"One People. One Planet. One Future."

AUTHOR

Michael Lerner, Ph.D., is president of Commonweal, a health and environmental research institute in Bolinas, California, and the Smith Farm Center for Healing and the Arts in Washington, D.C. He is a co-founder of the Collaborative on Health and the Environment and the Commonweal Cancer Help Program. He is the author of "Choices in Healing: Integrating the Best of Conventional and Complementary Approaches to Cancer" (MIT Press, 1994) and numerous essays. A former faculty member at Yale University, he received a MacArthur Prize Fellowship for contributions to public health in 1983.

Time to Get a Grip

BY MARTHA R. HERBERT, M.D., PH.D.

Does an environmental role in autism make sense? How do we decide?

And if environment *is* involved in autism, what do we do about it? These are challenging questions. Because our available information is complicated in many ways, each of us answers these questions based on our own judgment and deeply held worldviews.

We already know enough to take the environmental role in autism seriously. To say that the environment is involved in causing and triggering autism means that we believe that there have been new and different things going on in recent years, and that these developments have impact upon us. This is an easy claim to defend, and I will do that in this article.

To say that environmental factors can cause or trigger autism means that we have to look at the whole person and whole body, since environmental toxins and stressors will affect the whole body. This involves shifting from an older model that considers autism as a genetically determined "brain disorder" to a newer and more inclusive model that considers autistic behaviors as one of many effects of both genetic and environmental impacts on the whole person, including but not limited to the brain.[9]

This newer model of autism (or really, autisms, since there are many kinds of autism) implies that we have great opportunities to do constructive things about this challenge. To say that there are environmental causes and triggers of autism implies both that we can *prevent* the impairments associated with at least some kinds of autism, and that the suffering associated with at least some kinds of autism can be treated.

And finally, *it is time* for us to *get a grip* on this issue. If there is any chance at all that the autism of at least some people was *preventable* or is *treatable*, then *prediction* of risk, *prevention* of harm, and

reversal of injury all need to become top priorities. Moreover, environmental deterioration is a serious problem for everyone; understanding and handling it in autism may help many other challenges as well.

Why Autism and Environment?

It is often said that autism is the most highly genetic of the neurobehavioral disorders, and that there is little or no evidence of environmental factors.[28] However, observations about environmental factors relevant to autism go back decades, though they have been obscured in recent years by the dominance of a genetic focus. The view of autism as genetically determined is supported by observations of high "concordance" (matching autism diagnoses between identical twins) and high recurrence (increased chance of subsequent children having some kind of autism spectrum disorder after an autistic child is born into a family). In addition, a claim that autism is predominantly genetic rests on an assumption that our environment is stable and/or that we are not affected by environmental changes.

When we examine the frequently cited figure of a 90 percent "concordance rate" among identical twins (meaning that if one twin is autistic, there is a 90 percent chance that the other one will also be autistic), we can see that it overstates the case. Among identical twins, there is a 90 percent chance that if one twin is fully autistic, the other will have *some* autistic features, but only a 60 percent chance that the second twin will be *fully* autistic. While some researchers tend to focus on the 60 percent to make a case for genetic predisposition, we need to explain the 40 percent as well. To explain this nonconcordance we need to think about not just genes, but also the environment. Moreover, we also need to explain recent reports of high concordance among dizygotic (fraternal) twins, which suggest environmental rather than genetic factors.

We also know that the number of people diagnosed with autism has skyrocketed, both in the U.S. and in other countries. The current figures are running ten times higher than they were 15 or 20 years ago. The twin concordance data just discussed may not even apply to the new cases, since the studies were done before these increases were observed. Some say that the increases are merely due to better awareness and diagnosis of autism, or expanded diagnostic criteria. However, we would need solid proof of this claim in order to dismiss the possibility that something new, different and harmful is going on with our children—and such proof does not exist. Autism increases point to a role for the environment, since genes don't change that fast. The uncertainty and debate have not excluded the possibility that at least some portion of the increase in diagnoses is real. This gives us the responsibility to apply our serious and focused attention and resources to addressing what may be causing these alarming trends and what we can do about them.

The Big Picture: Major Environmental Changes

Let us now zoom out from autism and look at the bigger picture. If we assume that autism is mainly or purely genetic and not environmental, we are implying that nothing has changed in the environment that would alter genes or the ways that genes are expressed. Can we really defend the claim that the environment is stable? Hardly. Consider the following sample of unprecedented problems:

- In the past century there has been an exponential rise in the invention and production of new chemicals never before seen on the planet earth. Many of these are noxious and toxic by design (e.g. pesticides, industrial solvents), and many others have unanticipated toxic effects.
- We are facing a rise in a multitude of human illnesses including cancers as well as chronic, allergic, immune, autoimmune and degenerative illnesses.
- Among animals we are seeing a rise in infectious and cancerous illnesses and in malformations.
- We are losing biodiversity, with the greatest rate of extinction of plant and animal species since the Age of the Dinosaurs, not to speak of great loss of cultural diversity including the knowledge bases underlying many ecologically adaptive health-promoting traditions.
- There are a growing number of dead zones in the coastal oceans near large population settlements. Ocean pollution is enormous and we are seeing the dying out of fish stocks.
- Global climate change is becoming undeniable and appears to be proceeding faster than anyone had anticipated even a few years ago.

Addressing these and many more changes, a Millennium Ecosystem Assessment of the magnitude of the interlocking environmental crises we face was authored by more than 1,300 scientists from 95 countries and published early in 2005 by the United Nations and multiple partner organizations from around the world (www.millenniumassessment.org or www.maweb.org). Their "bottom line" summary sentence states, "We are spending Earth's natural capital, putting such strain on the natural functions of Earth that the ability of the planet's ecosystems to sustain future generations can no longer be taken for granted." From the vantage point of all of these unprecedented changes, there is no way to defend the claim that our environment is stable.

Given this pervasive environmental instability, we must ask ourselves, "Why would human children, and their developing brain and bodily systems, be spared?" In fact, given their delicacy, there is every reason to expect that children and their developing brains and bodies will be particularly affected.

Health Impacts of Environmental Change

Even in the face of widespread changes on our planet, some will still argue that there is uncertainty about whether these changes have health effects, as well as whether they could be causing or triggering autism. Is this a strong enough argument to justify inaction or delay? Not really. In committing to take notice and action, it is key to remember the saying, "Absence of evidence is not the same as evidence of absence." That is: a) just because something hasn't been thoroughly studied doesn't mean that nothing is going on, and b) the way you design a study has a big influence on the results you get.

Particularly important here is that we are learning many new things about how environmental exposures act upon our bodies that are forcing us to re-think how we decide what is safe and what is not safe. Michael Lerner discusses this "revolution in environmental health sciences" in his article, "Letter to a Friend Who Cares," which is in this issue. Two major areas of change are 1) how we define a "safe" level of exposure, and 2) what happens when we have many exposures in combination.

"Safe" levels: Recent science is showing us that chemicals at very low doses, many times beneath the previous "safety" thresholds, can cause harm—not by *killing* cells or living beings, but by mechanisms like *biomimesis—mimicking* the body's or organism's own signaling molecules. The most famous example of this is "endocrine disruption," in which chemicals such as those in pesticides or plastics can, in very small doses, act like hormones, and confuse the body's hormone regulation systems (for more information, see www.ourstolenfuture.org). Many people think that this might be relevant to autism, given that so many more boys than girls are affected and an altered hormonal environment might affect vulnerability.

Exposures in combination: We also are learning that combinations of exposures can have effects that could never be predicted from studying each exposure by itself. For example, researchers recently studied three chemicals found in the water in Brick Township, N.J., where an autism cluster was discovered. Each of these chemicals was individually determined at that time to be below toxic thresholds. However, in this experimental study, all three together damaged a pathway in brain development that each alone (or even in pairs) did not do.[19]

Together, these new scientific developments mean that we have probably hugely underestimated the health and ecological risks from environmental exposures.

We Are All Polluted

While it is surprising how little our "body burden" of chemicals has been studied, measurements show that we are all walking around with traces of at least hundreds of chemicals in our bodies. Even more alarming, babies are now *born* with traces of hundreds of chemicals in their bodies (for more information, see the October 2006 issue of *National Geographic*). Given the new science showing that chemicals in low doses and in combinations may have significant effects that can't be predicted from studying higher doses of single exposures, it appears that we are basically all living in uncharted territory regarding the health impacts of pollution in our own bodies.

Many Other Changes in Our Ways of Life

Chemicals are not the only new environmental exposures that we face. Many other exposures and stressors have emerged or greatly increased in the past century, including:

- Industrial farming: processed and refined foods; chemical pesticides and fertilizers; genetically modified foods
- Reproductive and hormonal manipulation
- The information revolution: media, computers and "information overload"
- Electromagnetic and nuclear radiation
- New-to-nature drugs, which may have long-term effects that take time to detect and would thus be missed in the standard short clinical trials that precede marketing
- Oral antibiotics, which change the ecology of intestinal microorganisms in unprecedented ways, and change the resistance properties of bacteria
- Air pollution and incineration disseminating many toxic substances—some new-to-nature
- Mechanically generated noise

It is possible to design studies in which any one of these changes is shown to have no significant effect in and of itself. However, it is also possible, and likely, that the combination of many of these exposures changes important aspects of our basic health. In this changed state, and particularly in the setting of genetic vulnerability, a further straw can break a camel's back. The impacts of combinations ofstressors are likely to be related to the rise in the number of people diagnosed with autism.[6]

Environment and Genetic Vulnerability

In the face of all of these environmental changes, we need to consider a different role for genes than outright determination of our health. Genes related to autism may not so much cause autism as set some people up to have greater vulnerability to factors that can trigger autism. This is a model of "gene-environment interaction," and it suits what we have learned to date better than a model of "genetic determination." Right now, we know of no genes that directly and inevitably cause autism. Even the genetic disorder Fragile X, which some people

describe as a "cause" of autism, is only associated with autism in 30 percent of cases, and therefore may be an extremely strong risk factor but still cannot be considered a "cause."

This "gene-environment interaction" model helps explain why it has been so hard to find "genes for autism." Some metabolic and signaling pathways are more involved with relating to the environment than others, and each such pathway involves many genes. The National Institute for Environmental Health Sciences is studying genes in such environmentally responsive pathways in its *Environmental Genome Project*.[20;30] Given the great variability in environments in which human beings have lived throughout our long history and migrations all over the planet, the many genes in these pathways are likely to show greater variability than other genes whose functions need to remain more stable across environments. We are already accumulating evidence of genetic differences in environmentally responsive genes, and environmentally responsive metabolic pathways in children with autism.[4;5;13;14;23] But any one environmentally responsive gene may have only a modest effect; and there may be many different combinations of such genes that lead to *vulnerability* to autism and a variety of exposures that alone or in combination may *trigger* the autism. This means we need fresh thinking about how we study genes and environment in autism. In particular this suggests that we need more study of environmentally responsive metabolic and signaling pathways, since these will guide us both to where to look for relevant genes, and also (to be discussed more below) to where to look for treatment targets. [11;13]

Can Regulation Keep Up With Science and Technology?

Currently, chemicals are studied only one at a time and there is no standard procedure for assessing low dose or combination effects. Moreover, a very large number of chemicals, those that were on the market before the institution of present regulations, have been "grandfathered" in, that is, allowed to be marketed without testing.

Amazingly, there is no requirement to test chemicals for their impacts on the developing nervous system, so that out of the approximately 3,000 chemicals produced in the largest volumes, *only 20-30* have been tested using the developmental neurotoxicology protocol.[8;25] For the rest, the painful truth is that we are flying blind. For combined exposures, even if we were to study *only* these top 3,000 chemicals in combinations of *only* three we would need to perform *85 billion tests,* which is basically impossible.

Recent science is teaching us much about the complexities of the ways that chemicals may act: differently in low than in high doses; differently in embryos and juveniles than in adults; differently in males than in females; and differently in relation to everyone's genetic individuality. In fact, genetic vulnerability to exposures can vary between individuals as much as 100- to 1,000-fold, or even more. As this new science advances, more and more scientists are realizing that our current screening tests for chemicals are not able to detect many newly appreciated classes of harmful effects.[24]

Finally, deciding how to assess exposures is a huge political battleground given the high economic stakes riding on the outcomes. This problem has received a lot of recent press in relation to the pharmaceutical industry but it is true of other industries as well. The politics of science and between scientists can greatly prolong the amount of time it takes to achieve consensus on updates in regulation, screening and scientific guidelines that might allow catch-up with new scientific research. Meanwhile, the marketplace is governed by outdated standards.

Autism, Genes, Environment and Medical Problems in Autism

Both genes and environmental exposures should not be expected to confine their effects to any one system in the body. Virtually all of the cells in our bodies have the same genome and many of the body's core biochemical processes (which are shaped by genes) occur in many or all of our bodily systems. Therefore, a genetic change may express itself in many bodily systems and an environmental exposure may target a biochemical vulnerability that is widely distributed in the body. The separation of the brain from the body is really an artificial distinction. All of our bodily systems are interconnected.

Some bodily systems more directly interface with the environment, such as the gastrointestinal system, which is the first port of entry of many environmental exposures, and the immune system, which deals with responses to outside intrusions into the body. From the perspective of gene-environment interactions, it should come as no surprise that we are seeing gastrointestinal and immune problems in many autistic individuals.

Autism as a Whole-Body Condition

It may well be that the medical problems in autism are not incidental or extra problems "on top of" the autism but rather core parts of the problem. They may well be manifestations of systemic biological disruptions that lead, at the level of brain output, to behaviors that meet criteria for "autism," and also, at the same time, lead to various kinds of bodily illness—digestive system problems, allergies, sleep disruptions, seizures, sensory disturbances, low muscle tone, clumsiness and a variety of other problems that in various combinations affect many people with autism.

When people think about autism, they often think of the brain problems as primary and call it a "neurobiological" disorder. No doubt the brain is involved in producing atypical behaviors. However, from the perspective of gene-environment

interactions, we need to ask whether the brain is the primary target, or whether the brain could be affected at the same time as—"in parallel" with—or even "downstream" of, other bodily changes, such as in the immune system. Perhaps the brain is "caught in the crossfire" of whole-body changes related to environmental stress.

Could Brain Changes in Autism Reflect Environmental Impacts?

Once we consider environmental impacts on autism, important questions are raised about how we interpret the changes we have seen so far in brains of people with autism. It is certainly true that researchers have documented brain differences in individuals with autism. One way of interpreting these changes is to presume they are genetically based, and therefore to look for correlations between genes, the regions of the brain that show changes, and the types of behaviors we see in autism. However, another way of thinking about brain changes in autism is to use the evidence as clues to help figure out what biological mechanisms are driving the problems.[12] Recently researchers have been documenting evidence of inflammation and oxidative stress in the brain.[21;26;27] These kinds of changes are well known to be two of the main ways that the body and brain respond to an overload of metabolic and environmental stressors. There are also other changes that have been documented in brains from people with autism that can increase the brain's "excitability" (i.e., intensity of response to stimuli).[22] Such changes can be caused by both genetic and environmental factors, which alone, or even more, in combination tip the system in the same "excitable" direction. There are also various possible ways that environmental impacts could be related to other brain changes researchers have documented, such as larger brain size and reduced brain coordination, as well as limbic system and cerebellar changes.[10;15] These brain changes and their impacts are hard to explain by a purely "genetic determination" model. A "gene-environment interaction" model works better. And since the brain—which after all is a wet organ of the body and not just an information-processing computer—may be "downstream" of other body changes, a brain-body interaction model may explain more changes than looking at the brain by itself.

The important thing to remember here is that we don't need to make an "either-or" choice between "gene and environment" or "brain and body;" instead, we need to take a "both-and" approach, and learn how the members of each pair work together.

Autism and the Environment: Can We Find the Cause?

We have sketched the overall picture that many dramatic changes are happening in our environment that may be contributing to the dramatic increases we are seeing in autism. Can we argue that among all of the environmental factors there is a single exposure, infectious agent or stressor that uniquely accounts for the rise of autism? So far, studies have not established strong support for this theory. At the same time, there may be some environmental exposures, such as heavy metals, that contribute more strongly than others. Getting answers to the question of cause is important for two main reasons. The first is that if we find out what is causing harm, we can work on preventing future harm. The second is that if we understand the mechanisms by which particular causes or triggers contribute to autism, we can work on targeted biomedical treatments that halt or even reverse the injuries.

Environment and Final Common Pathways

Realistically, it will probably be quite a while before we definitively establish cause, if we ever do. What are we to do right now about helping individuals in a whole-body way with their whole-body autism? How do we know where to start, given the likelihood of prolonged disagreement and debate about both body and environment in autism, as well as the huge number of poorly tested chemicals and other stressors and the essentially infinite number of combinations in which we can be exposed to them—plus variations in the timing of when we are exposed? In some respects our bodies make it a little easier for us, in that we only have a finite number of metabolic pathways through which we handle and eliminate environmental exposures and stress. This means that many different factors converge onto a smaller number of body systems, which are "final common pathways" for environmental responsiveness. From this vantage point, researching and treating the body's mechanisms for handling and eliminating environmental stressors is central to strategies for treating and preventing the impairments of autism.

Autism Recovery: Plausible in the Gene-environment Model

We are hearing a growing number of reports of children recovering substantially or completely from their autism. Recovery does not mean leaving behind the gifts and creativity that can accompany autism, but instead, leaving behind the physical suffering and narrowed options associated with impairments. Some of these recoveries are attributed to intensive behavioral therapy; some to intensive biomedical intervention; and many to a combination of both. Although autism has traditionally been considered incurable, the "incurability" is merely an assumption—it has never been scientifically proven.

From a gene-environment, whole-body approach, it makes sense to consider the possibility of recovery from autism to be

scientifically plausible. Environmental causes and triggers are not inevitable, and many of their effects may be reversible. In particular, environmental exposures can change brain function (for example, brain metabolism, coordination and signaling properties) and not just hard-wired brain structure. Treatments including stress reduction (e.g. from behavioral interventions) as well as biomedical treatments can improve aspects of brain function. In principle, this opens the possibility of improvement and successful treatment. As we learn more details of brain-body interactions in autism, we can expect a clearer picture of how we can improve brain function not only by treating brain and behavior, but also by treating body problems that impact the brain.

Currently efforts are underway to study autism recovery,[7;18] and to see whether we can find cases where claims of autism recovery can be rigorously documented by reliable testing before and after treatment. These efforts parallel those that were needed to rigorously document autistic regression before many people would believe that it could occur.[29] We can also study recovered children to answer some critical questions. We need to know whether there is something different about the children who improve or recover, or whether the recovered children were just lucky to receive the combination of treatments that worked for them. Either way, we need to know how to predict which treatments will be right for each child and to optimize treatment protocols.

Final Common Pathways and Autism Recovery

Many biomedical interventions in autism, particularly non-pharmacological and "non-traditional" approaches such as nutritional supplementation and elimination diets, have seemed paradoxical and peculiar from the vantage point of autism viewed as a genetically determined brain disorder. However, when we examine these approaches from the gene-environment, whole-body model's perspective, we see that they are designed to target the body's "final common pathways" of response to environmental exposures and stressors.

Two common non-drug biomedical interventions are nutritional supplementation (adding what is insufficient)[1] and elimination diets (removing what is irritating). Nutrients are co-factors that, among many other things, assist in the body's biochemistry of detoxification. Many nutrients are depleted in a diet of industrially-produced processed foods as well as poorly absorbed in the presence of gastrointestinal disturbances. This leads to nutritional insufficiencies that occur at the same time as exposure to toxins and other stressors increase the body's need for these very nutrients. Moreover, explosively burgeoning research in the field of nutrigenomics is uncovering reasons for huge differences in nutritional needs between individuals,[17] meaning that some people will be more sensitive to nutrient depletion than others, and some individuals will require greater quantities of nutrients than others to meet either their basic needs or even more, their nutrient needs under stress.[2] Elimination diets attempt to remove stressors that irritate and inflame an already struggling immune system.[16] Both of these interventions (and others as well) are aimed at improving the body-brain's resilience—its ability to function, regulate itself, and handle environmental and emotional stressors.

Not all of these biomedical approaches work for every individual with autism. Part of the problem in applying and evaluating biomedical treatments is that children can arrive at autism through many different underlying biological routes, leading to the need for a range of different treatment approaches. If treatments are evaluated on a group of autistic children who have different underlying biological causes and mechanisms, then evidence that approaches are successful for some sub-groups will be washed out by averaging these good responses with poor responses in children whose biology is different. Another challenge is that many autistic children appear to have a lot of interacting metabolic disturbances, making the treatment of one problem at a time less effective than treatments for several facets of the condition that are given in combination. This is a problem for clinical research, where clinical trials usually involve studying one treatment at a time. Effective research on these autism treatments, like effective research in many other domains where our appreciation of complexity is growing (e.g. genomics, metabolomics, nutrigenomics), will require innovation in study design methods.

> "How do we know where to start, given the likelihood of prolonged disagreement and debate about both body and environment in autism..."

Autism as a Case Study of Environmental Illness and Treatment

It has been proposed that autism has features in common with other neurological diseases such as Alzheimer's and Parkinson's disease (particularly the environmental responsiveness and brain inflammation that all three conditions appear to share)

and with other illnesses with strong environmental components such as various immune and autoimmune diseases. The idea that different disease diagnoses that occur at different points in the lifespan may share some common underlying mechanisms is gaining more support.[3] This means that more work needs to be done not just on the behavioral overlaps between autism and other neuropsychiatric disorders (e.g. obsessive-compulsive disorder, language impairment), but also on the physiological overlaps (e.g. metabolism, biochemistry, immune system, exposure history) between autism and other disorders. This is relevant to developing treatments. For example, the drugs memantine (approved for treatment of the symptoms of Alzheimer's disease related to brain excitability), minocycline (used in Alzheimer's, Huntington's Disease and Parkinson's disease to reduce brain inflammation) and pioglitazone (approved for diabetes and associated with reducing immune activation) are now in clinical trials for autism treatment. Treatments that target symptoms or underlying functional problems may be helpful for more than one condition. Thus, advances in research and treatment in autism may both help and benefit from advances in research and treatment of other conditions. And all of these environmentally modulated illnesses will benefit from making our environment safer and healthier.

Autism as a Wake-up Call

The rise in autism diagnoses, along with the rise in other immune and chronic illnesses, is really a wake-up call. Put alongside the warnings about the ecological instability of our planet, it shows that our situation is serious. It calls for pulling out all the stops and throwing our best intelligence, resources and organization into *getting a grip*. Autistic individuals may not be "different" from the rest of us but simply "more sensitive" to environmental injury—they may be the "canaries in the coal mine" warning us of impending greater disaster. If the level of environmental insults continues to rise, more children and more adults—and more of life on earth—will experience harm.

Toward Regrouping our Priorities and Getting a Grip

Being touched by autism is a life-transforming experience. It makes huge demands on our time, and it forces us to think "outside the box" and across boundaries in order to rise to its challenges. It requires partnerships of many kinds—doctors with parents, scientists with clinicians and patients, parents with their autism spectrum children, schools with health care providers, governments with communities, and more—all of which call for ongoing creativity. It also requires a willingness to face painful realities about the limits to our knowledge and resources, and about many mistakes we did not know we were making. Dealing with autism on an everyday basis forces us to act on our best *judgment* even when critical areas of precise knowledge are lacking.

All of this is true as well of what we are facing and will increasingly face regarding the deterioration of our environment. Environmental deterioration will affect the health of a growing portion of the population and the earth's living and physical systems. It will be life-changing in profoundly inconvenient, time-consuming and disturbing ways. It is hugely complex and so will probably forever defy our efforts to define it with final precision. We can learn many things from our struggle to improve the health and functioning of autistic individuals that will empower us in facing other health and environmental challenges as well. We already have enough evidence to make the judgments that environmental factors are critical issues for autism. It is in all of our best interests to come to grips with these challenges now.

> "Autistic individuals may not be 'different' from the rest of us but simply 'more sensitive' to environmental injury..."

Autism may well be one of many forms of "collateral damage" from our uncritical trust in "progress," and in particular our unawareness of the many cascading "side" effects of our clever inventions (or, more accurately, "other" effects than those we intended with our narrow and short-sighted "cause-effect" models). This kind of damage challenges us to intelligently regroup our priorities without delay, and to learn the skills of keeping in mind complexity and interconnection. If we make an earnest effort now, perhaps we can avert irreversible stress on our health and our environment, and move instead toward more humane, sustainable ways of living that promote not harm, but the health and fulfillment for which we all yearn.

Turning our priorities now toward predicting risk, preventing harm and reversing injury in autism and in other environmental illnesses, and pursuing these policies in the setting of the broadest and most forthright awareness of the magnitude of the difficulties we face, will provide us with a positive focus that can bring us together in this time of great challenge and danger.

AUTHOR

Martha Herbert, M.D., Ph.D., is an assistant professor of neurology at Harvard Medical School, and a pediatric neurologist at the Massachusetts General Hospital in Boston and Cambridge Health Alliance Center for Child and Adolescent Development. She received her medical degree from Columbia University College of Physicians and Surgeons, did her pediatric training at Cornell University Medical Center in New York City and her neurology training at the Massachusetts General Hospital. Prior to her medical training, she earned a Ph.D. in the History of Consciousness at the University of California, Santa Cruz. She studies brain size and brain coordination problems in autism, how body problems affect the brain and how researchers can measure changes in brain function that can result from treatment interventions.

REFERENCES

1. Ames BN. The metabolic tune-up: metabolic harmony and disease prevention. J Nutr 2003 May;133(5 Suppl 1):1544S-8S.
2. Ames BN, Elson-Schwab I, Silver EA. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K(m)): relevance to genetic disease and polymorphisms. Am J Clin Nutr 2002 Apr;75(4):616-58.
3. Becker KG. The common variants/multiple disease hypothesis of common complex genetic disorders. Med Hypotheses 2004;62(2):309-17.
4. Buyske S, Williams TA, Mars AE, Stenroos ES, Ming SX, Wang R, Sreenath M, Factura MF, Reddy C, Lambert GH, et al. Analysis of case-parent trios at a locus with a deletion allele: association of GSTM1 with autism. BMC Genet 2006 Feb 10;7(1):8.
5. D'Amelio M, Ricci I, Sacco R, Liu X, D'Agruma L, Muscarella LA, Guarnieri V, Militerni R, Bravaccio C, Elia M, et al. Paraoxonase gene variants are associated with autism in North America, but not in Italy: possible regional specificity in gene-environment interactions. Mol Psychiatry 2005 Jul 19.
6. Daniels JL. Autism and the environment. Environ Health Perspect 2006 Jul;114(7): A396.
7. Fein D, Dixon P, Paul J, Levin H. Pervasive Developmental Disorder Can Evolve Into ADHD: Case Illustrations. J Autism Dev Disord 2005;35:525-34.
8. Goldman LR, Koduru S. Chemicals in the environment and developmental toxicity to children: a public health and policy perspective. Environ Health Perspect 2000 Jun;108 Suppl 3:443-8.
9. Herbert MR. Autism: A Brain disorder or a disorder that affects the brain? Clinical Neuropsychiatry 2005;2(6):354-79.
10. Herbert MR. Large brains in autism: the challenge of pervasive abnormality. Neuroscientist 2005 Oct;11(5):417-40.
11. Herbert MR, Russo JP, Yang S, Roohi J, Blaxill M, Kahler SG, Cremer L, Hatchwell E. Autism and environmental genomics. Neurotoxicology 2006 Sep;27(5):671-84.
12. Herbert MR, Ziegler DA. Volumetric Neuroimaging and Low-Dose Early-Life exposures: Loose Coupling of Pathogenesis-Brain-Behavior Links. Neurotoxicology 2005;26(4):565-72.
13. James SJ, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, et al. Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. Am J Med Genet B Neuropsychiatr Genet 2006 Aug 17.
14. Johnson WG. Teratogenic alleles and neurodevelopmental disorders. Bioessays 2003 May;25(5):464-77.
15. Just MA, Cherkassky VL, Keller TA, Minshew NJ. Cortical activation and synchronization during sentence comprehension in high-functioning autism: evidence of underconnectivity. Brain 2004 Aug;127(Pt 8):1811-21.
16. Jyonouchi H, Geng L, Ruby A, Reddy C, Zimmerman-Bier B. Evaluation of an association between gastrointestinal symptoms and cytokine production against common dietary proteins in children with autism spectrum disorders. J Pediatr 2005 May;146(5):605-10.
17. Kaput J, Ordovas JM, Ferguson L, van Ommen B, Rodriguez RL, Allen L, Ames BN, Dawson K, German B, Krauss R, et al. The case for strategic international alliances to harness nutritional genomics for public and personal health. Br J Nutr 2005 Nov;94(5):623-32.
18. Kelley E, Fein D, Naigles L. Language functioning in optimal outcome children with a history of autistic spectrum disorders. J Autism Dev Disord In press.
19. Kreiling J, Stephens R, Reinisch C. A mixture of environmental contaminants increases cAMP-dependent protein kinase in *Spisula* embryos. Environmental Toxicology and Pharmacology 2005;19:9-18.
20. NIEHS. Environmental Genome Project, National Institute of Environmental Health Sciences. http://www.niehs.nih.gov/envgenom/ .
21. Perry G, Nunomura A, Harris P, siedlak S, Smith M, Salomon R. Is autism a disease of oxidative stress? Oxidative Stress in Autism Symposium, New York State Institute for Basic Research in Developmental Disabilities, Staten Island NY, 2005 Jun 16;p. 15.
22. Rubenstein JL, Merzenich MM. Model of autism: increased ratio of excitation/inhibition in key neural systems. Genes Brain Behav 2003 Oct;2(5):255-67.
23. Serajee FJ, Nabi R, Zhong H, Huq M. Polymorphisms in xenobiotic metabolism genes and autism. J Child Neurol 2004 Jun;19(6):413-7.
24. Slotkin TA. Guidelines for developmental neurotoxicity and their impact on organophosphate pesticides: a personal view from an academic perspective. Neurotoxicology 2004 Jun;25(4):631-40.
25. Stein J, Schettler T, Wallinga D, Valenti M. In harm's way: toxic threats to child development. J Dev Behav Pediatr 2002 Feb;23(1 Suppl):S13-22.
26. Vargas DL, Nascimbene C, Krishnan C, Zimmerman AW, Pardo CA. Neuroglial activation and neuroinflammation in the brain of patients with autism. Ann Neurol 2005 Jan;57(1):67-81.
27. Vargas DL, Bandaru V, Zerrate MC, Zimmerman AW, Haughey N, Pardo CA. Oxidative stress in brain tissues from autistic patients: Increased concentration of isoprostanes. IMFAR 2006 2006 Jun: Poster PS2.6.
28. Veenstra-Vanderweele J, Christian SL, Cook EH Jr. Autism as a paradigmatic complex genetic disorder. Annu Rev Genomics Hum Genet 2004;5:379-405.
29. Werner E, Dawson G. Validation of the phenomenon of autistic regression using home videotapes. Arch Gen Psychiatry 2005 Aug;62(8):889-95.
30. Wilson SH, Olden K. The environmental genome project: phase I and beyond. Mol Interv 2004 Jun;4(3):147-56.

Stepping Stones

Center for Autistic Spectrum Disorders, Inc.

www.steppingstonesca.com

"dedicated to improving the lives of children"

Stepping Stones Center for Autistic Spectrum Disorders, Inc. is a Non-Public Agency (NPA) that designs individualized behavioral, educational, social, speech-language and occupational therapy programs for individuals diagnosed within the autism spectrum and other related disorders. Our full range of services include but are not limited to: onsite behavior management consultation and implementation; full inclusion services; emphasizing learning by offering a positive and proactive learning approach to challenging behaviors through the use of behavior management strategies to effect positive change; developing teaching strategies through a systematic assessment of each child's learning environment using clear, measurable goals and detailed performance data to maximize success; providing strategies for successful collaboration among all members of the individual's educational environment; speech-language therapy (including two center-based programs for children ages 18 mos.-5 years in selected branch locations); occupational therapy (in selected branch locations) and summer acting camp services.

Stepping Stones understands the importance for continued parent support and the need for parents to connect with other parents who have similar needs. For this reason, Stepping Stones has implemented a "Parent Educator" service (free of charge to any parent) in order to provide such assistance and support to not only our clients but to other families in the community, with related needs, who have children diagnosed within the autism spectrum. We, at Stepping Stones, have two parent educators on staff, (who are also parents of children diagnosed within the autism spectrum). These parent educators are available to speak with families and help answer questions or address concerns they may have regarding their child's needs. In addition, these parent educators will attempt to contact clients on a monthly basis as a form of "checking in" to make sure that the child's home-based program is running smoothly and to help answer any questions or concerns that families may have in order to ensure prompt attention and immediate action to address such matters.

Our parent educators may also refer families to other helpful resources in order to help them address their child's needs. It is important to note that our parent educators are not legal advocates nor do they represent themselves as "professional experts" in Autism or in any related field to Autism. Therefore, all legal questions and any other questions that would be best addressed by a certified, licensed, or credentialed professional should be addressed to those with such credentials that provide such services in this field.

Please visit our website at www.steppingstonesca.com for more information.

Beyond Behavior—
Biomedical Diagnoses in Autism Spectrum Disorders

BY MARGARET L. BAUMAN, M.D.

©NANCY LOUIE

The autism spectrum disorders (ASD) are behaviorally defined disorders characterized by impaired social interaction, delayed and disordered language and isolated areas of interest. Symptoms can vary over time and with functional level but may include poor eye contact, insistence on sameness, atypical cognitive development, repetitive and stereotypic behaviors, deficits in joint attention and a normal physical appearance.

Although the cause of ASD remains unknown, there is strong evidence that genetics plays a significant role. Although once considered rare, current prevalence rates suggest that one in every 166 children may be affected with ASD (Fombonne, 2003).

Since the initial description of infantile autism by Dr. Leo Kanner in 1943, much of the clinical research related to the ASDs has centered on investigations of cognition, behavior, social skills and language, with relatively little attention to the possible significance of associated medical conditions. Physical examination of ASD children can be challenging and often is limited by poor patient cooperation and difficult office behavior, as well as the fact that many of these children are nonverbal and therefore unable to describe or localize discomfort. In addition, some of these children may present with symptoms that are atypical and whose causes are not easily recognized. Research suggests that children with ASD are less likely than those with mental retardation or other special needs to obtain specialty medical care.

The fact that a child has autism does not rule out the possibility that he may have one or more other illnesses or disorders, similar to those that affect typically developing children.

Failure to diagnose and treat these disorders may compromise the child's ability to function in a classroom and to take advantage of therapeutic services; negatively impact quality of life for the child and his family; and, in some cases, even lead to hospitalization and perhaps death. In addition, identifying associated medical disorders may amplify the phenotypic description (observable traits or characteristics of a living being) of subsets of ASD children, and defining these subsets may have genetic implications.

Space does not allow a detailed description of the multiplicity of medical conditions that may affect the child with autism. Therefore, only some of the more common disorders will be highlighted here. These include seizures, sleep disturbances and gastrointestinal disorders, with brief comments regarding metabolic, urologic and hormonal dysfunctions. This is not an all-inclusive list, and the primary care physician and specialist working with ASD children must remain alert to a wide range of medical possibilities at any one time.

Seizure Disorders. Seizure disorders are said to affect approximately one third of people with ASD at some time during their lives, with peak risk periods in early childhood and during adolescence (Volkmar and Nelson, 1990). No one seizure type has been reported to be specifically associated with autism, and most electroencephalographic (EEG) and seizure patterns have been observed in ASD.

As with typically developing children, if seizures are suspected, appropriate diagnostic procedures, including the performance of an EEG, should be implemented, the type(s) of seizures identified and treatment started. In some cases, the onset of seizures may signal the need for more extensive evaluations and specialty referrals to rule out underlying metabolic disorders, syndromes, degenerative disorders, head trauma or mass lesions.

Atypical behavioral patterns and body movements often can be observed in children with autism, complicating the ability to accurately diagnose a potential seizure disorder. But not all body movements or mannerisms observed in ASD children are seizure-related. Some may be related to other medical conditions, such as gastroesophageal reflux disease (GERD) or other gastrointestinal disturbances (Buie, 2005). Thus, carefully analyzing the behaviors of concern is critical to targeting the most appropriate and, therefore, effective treatment. Since the child does not usually exhibit the concerning behaviors during the office visit, ask the family or the school to obtain a videotape of these events for diagnostic purposes.

Sleep Disorders. Sleep disorders are said to occur in approximately 30 percent of typically developing children and appear to be more common in early childhood (Ferber, 1996). Sleep disturbances include delayed sleep onset, frequent nighttime awakenings, sleeping too much, nightmares or night terrors. Among children with autism, parents most frequently report difficulty getting to sleep, frequent nighttime awakenings and/or early morning arousals followed by the child remaining awake for the day.

While the causes of sleep disturbances may be related to central nervous system dysregulation of arousal and/or abnormal REM sleep patterns, physicians and families should consider the potential contribution of enlarged tonsils and adenoids, or gastroesophageal reflux. Urinary tract infections associated with nocturnal enuresis (bed-wetting) also could contribute to nighttime awakenings. Because there is growing evidence that disordered sleep can negatively impact daytime behavior and learning, it is important to determine the cause of the sleep disturbance and treat the underlying condition.

Gastrointestinal Disorders. Parents frequently describe gastrointestinal disorders—usually diarrhea, chronic constipation, food intolerances, gas, bloating and abdominal pain/discomfort—as issues for children with ASD. However, the percentage of children with autism suffering from GI disorders is not known; nor is it known whether these disorders are more common in ASD than in typically developing children. Disorders such as celiac disease, gastroesophageal reflux, colitis, esophagitis, gastritis, food allergies and motility dysfunction have all been reported in those with ASD.

"The fact that a child has autism does not rule out the possibility that he may have one or more other illnesses or disorders, similar to those that affect typically developing children."

Although typical GI symptoms often are apparent in some children with ASD, others may present with episodes of aggression and/or self-injurious behavior (SIB) without evidence of GI symptoms. These behaviors are observed most frequently in lower-functioning children who are nonverbal and who have no other means of expressing their discomfort or pain. Well-designed research is needed to define the prevalence of GI disturbances in ASD, the types of disorders most often found, and the signs and symptoms with which these children present. It is important to consider gastrointestinal dysfunction in ASD, especially in those children who are nonverbal or hypoverbal, and who have developed behavioral outbursts without obvious cause.

Metabolic Disorders. Metabolic disorders only recently have become a potentially important area of investigation in ASD.

Several reports have suggested, for example, an association between ASD and mitochondrial disorders (Oliveira et al., 2005; Miles et al., 2005). Possible clinical "red flags" that may suggest such a diagnosis include low muscle tone, easy fatigability and poor physical endurance, and repeated regressions. If there is a suspicion of an underlying metabolic disorder, a referral to a medical geneticist should be considered, since some of these disorders are treatable.

Hormonal Imbalance. Hormonal imbalance has been found in some children with autism, most often during preadolescence and adolescence. Precocious puberty has been reported in both ASD boys and girls. Behavioral disruptions that seem to have a relationship to the onset of the menstrual period should suggest the possibility of disordered estrogen/progesterone levels and a referral to an endocrinologist could be beneficial.

Other Concerns. Other health care concerns include recurrent ear infections, hearing impairment, urinary tract infections, spastic bladder leading to new onset of bedwetting at any age, attention deficit hyperactivity disorder, disordered sensory processing and almost any other illness commonly seen in typically developing children.

Regardless of the challenging behaviors with which many ASD children present, the physician must remain mindful of the fact that these children may have any number of common childhood illnesses and disorders, but their presentation may be atypical and thus may create a diagnostic dilemma, especially in very young children and in those who are nonverbal. However, many of these medical conditions are treatable, and effective diagnosis and intervention can substantially improve the child's daytime behavior, his attention and ability to learn, and his overall quality of life as well as that of his family. Quality health care should be considered a high priority for all children with autism. Their futures may depend on it.

AUTHOR

Margaret L. Bauman, M.D., is associate professor of neurology at Harvard University Medical School; adjunct associate professor of anatomy and neurobiology at Boston University School of Medicine; associate pediatrician and assistant neurologist at Massachusetts General Hospital, and medical director of the Autism Treatment Network. She also directs LADDERS (Learning and Developmental Disabilities Evaluation and Rehabilitation Service), a satellite multidisciplinary clinic of the Massachusetts General Hospital for Children, and both the Autism Research Foundation and the Autism Research Consortium. In California, Bauman serves as a child neurology consultant for the Casa Colina Centers for Rehabilitation Inc, in Pomona, Calif., and as a volunteer physician for the department of pediatrics at the University of California, Irvine. Her research interests include the study of the microscopic brain structure in autism, Rett syndrome and other disorders of neurological development. Bauman has more than 75 scientific publications, including peer-reviewed journal articles, book chapters and books. The 2nd edition of her book, The Neurobiology of Autism, *co-edited with T.L. Kemper, was released in January 2005.*

REFERENCES

Buie, TM. Gastrointestinal issues encountered in autism. In: Bauman, ML and Kemper, TL, eds. *The Neurobiology of Autism.* Johns Hopkins University Press: Baltimore. Pp. 103-117, 2005.

Ferber, R. Childhood sleep disorders. Neurologic Clinics. 14:493-511, 1996.

Fombonne, E. The prevalence of autism. J.Am Med Assoc. 289:87-89, 2003

Kanner, L. Autistic disturbances of affective contact. Nervous Child. 2: 217-250, 1943.

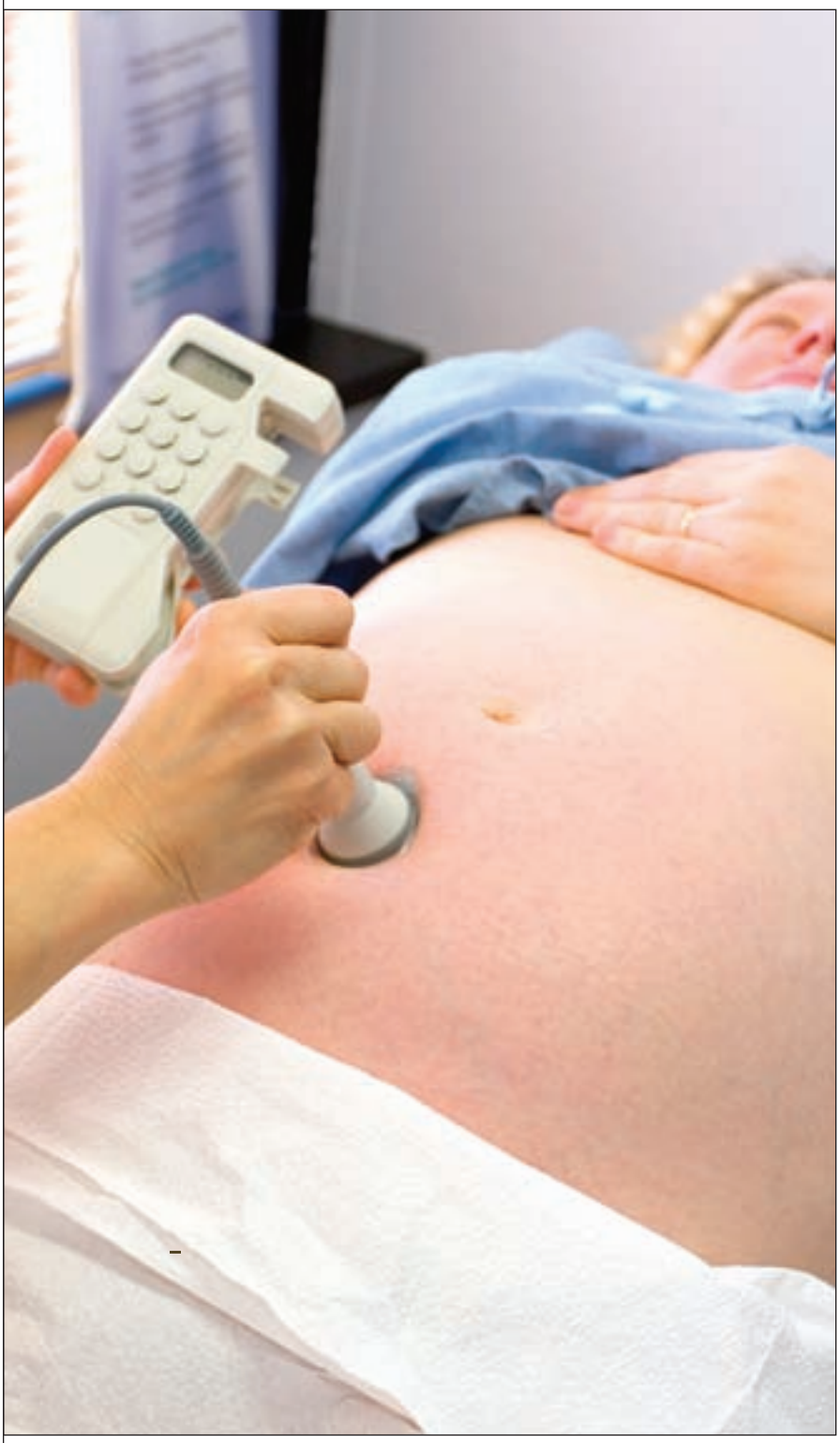
Miles, JH, Takahasi, TN, Bagby, S, Sahota, PK, Vaslow, DF, Wang, CH, Hillman, RE, Farmer, JE. Essential versus complex autism: definition of fundamental prognostic subtypes. Am J Med Genetics. 135A(2):171-180, 2005.

Oliveira, G, Diogo, L, Grazina, M, Garcia, P, Ataide, A, Marques, C, Miguel, T, Borges, L. Vicente, AM and Oliveira, CR. Mitochondrial dysfunction in autism spectrum disorders: a population-based study. Dev Med Child Neurol. 47:148, 2005.

Volkmar, FR and Nelson, DS. Seizure disorders in autism. J. Amer Acad Child Adolesc Psychiar. 29:127-129, 1990.

The Prenatal Environment and Neuroinflammation in Autism

BY SUSAN L. CONNORS, M.D., CARLOS A. PARDO, M.D. AND ANDREW W. ZIMMERMAN, M.D.



The neurobiological basis for autism remains poorly understood. However, research suggests that environmental and immunological as well as genetic factors are contributors.

Although most studies of the circulating immune system have found differences in autism, until recently studies of the brain have demonstrated few signs of immune activity. Our studies showed neuroinflammation (activation of neuroglia, immune cells called microglia and astroglia) and an increase in cytokines (immune chemicals) in the brains of autistic patients compared to controls.

Neuroglia are important in neuronal (nerve cell) function. Astroglia contribute to detoxification, produce growth factors, and secrete pro- or anti-inflammatory substances after injury or in response to neuronal dysfunction. Microglia are involved in responses to injury or dysfunction, and contribute to development of connections between neurons and the ability of the immune system of the brain to detect abnormal cells.

Both astrocytes and microglia are important in the developing brain, and alterations in their function can produce changes likely to contribute to brain dysfunction in autism. The neuroinflammation we found may result from external exposures, or from abnormal functioning of these or other brain cells.

Our research group is interested in the pregnancy environment in the development of autism. Maternal antibodies, produced by immune cells after external exposures, are of particular interest because they may affect fetal brain development.

The late Dr. Reed Warren and his colleagues originally demonstrated reactivity of mothers' blood serum to their autistic children's lymphocytes, meaning that the mothers' immune systems responded to these blood cells in the children as though they were "invaders." Similarly, maternal serum can cause antibody binding to Purkinje cells (a type of nerve cell that possesses a great deal of control over the refinement of motor activities) in

the cerebellum of the fetus—evidence of an immune reaction—when injected into pregnant mice.

Autoimmune disorders associated with antibodies, such as rheumatoid arthritis, lupus and thyroid disease, are increased among mothers and other family members of autistic children. Maternal antibodies, therefore, may influence fetal brain development during pregnancy by interfering with cell signaling in the developing brain and disturbing its organization. These antibodies also might result from environmental exposures in susceptible mothers during pregnancy.

Although it has been tempting to link abnormalities in circulating cells of the immune system in autism with differences in the brain, this has never been proven. Immune activation reported in autism brain and circulating immune system differences are more likely to develop in parallel, due to disturbances in mechanisms affecting development of both systems in the fetus.

All neurotransmitter systems interact to produce normal prenatal brain maturation, and abnormalities in one may impact the development of others. One example involves the B2AR (beta-2 adrenergic receptor), which is important for normal brain and tissue maturation. We have linked overstimulation of this receptor by terbutaline, a drug used for preterm labor, with concordance for autism in nonidentical twins. ("Concordance" for autism means that both twins have the disease, while "discordance" means that one does while the other does not.)

Our study found that half of the twin pairs concordant for autism had been exposed to terbutaline for two weeks or more, while only six of the 24 discordant pairs had been exposed to the drug for an extended period. We also found an increased frequency of specific polymorphisms, or variants of the B2AR gene, that may increase the susceptibility to autism.

Animal studies show that treatment of pregnant rats with terbutaline results in offspring with changes in the brain analogous to those in autism. Overstimulation of the B2AR with terbutaline, at an age in rats equivalent to the second trimester in humans, has also resulted in postnatal B2AR cell signaling in brain and other tissues of the offspring that is similar to the signaling that normally occurs during the fetal stage but not after birth. If this animal model proves comparable to autism, the abnormal persistence of fetal patterns of development could contribute to immune activation in the autism brain, and circulating immune system differences reported in this disorder.

Our group found neuroinflammation in this rat model of prenatal B2AR overstimulation, which can be used to investigate how neuroglial activation arises and persists beyond fetal brain development. We also found protein and lipid markers of oxidative stress in autism brain tissue. This finding may reflect a fetal pattern of cell functioning, in which tissue responses are too immature to handle "normal" exposures after birth.

It is important to note that the cellular effects from overstimulation of the B2AR may be an important process in the development of autism, more than terbutaline exposure alone, because additional factors, such as maternal stress, infections, heavy metal and pesticide exposure also might produce similar results. Interestingly, interference with B2AR signaling during fetal life may result in a "set-up" for susceptibility to environmental exposures after birth. Dr. Melissa Rhodes and colleagues at Duke University have shown that terbutaline exposure in rats (at the same age equivalent as above) *followed by* postnatal exposure to chlorpyrifos (a pesticide) results in synergistic, additive abnormal effects in brain and other tissues.

Interference with neurotransmitter signaling, such as the case with terbutaline and the B2AR system, may have relevance to findings from research on the immune system in autism. Disordered development of one important transmitter system may result in failure of the orderly maturation of others, resulting in increased susceptibility to environmental factors.

AUTHORS

Susan L. Connors, M.D., is a board certified internist who has been doing research in the field of autism at the Kennedy Krieger Institute, while raising an autistic son. Connors has completed a study of prenatal drug exposure in twins with autism, using a clinical sample and the Autism Genetic Resource Exchange, and a study of polymorphisms of the beta 2 adrenergic receptor in fraternal twins with autism spectrum disorders.

Carlos A. Pardo-Villamizar, M.D., is an assistant professor of neurology and pathology (neuropathology) at the John Hopkins University School of Medicine. He is also co-director of the Transverse Myelitis Center, staff neurologist of the Multiple Sclerosis Center and member of the HIV Neurosciences Research Group at the Johns Hopkins Hospital.

Andrew Zimmerman, M.D., is a pediatric neurologist and research scientist at the Kennedy Krieger Institute. He is also an associate professor of neurology and psychiatry at the John Hopkins University School of Medicine.

Gastrointestinal Illness in Autism:

An Interview with Tim Buie, M.D.

BY KULANI MAHIKOA

© DUSTIN STELLER MODEL DOES NOT HAVE AUTISM.

"Gastrointestinal [GI] illness is not uncommon in autistic individuals," said Tim Buie, M.D., pediatric gastroenterologist at Massachusetts General Hospital (MGH). He speaks from experience. To date, Buie and his team at MGH have performed more than 2,000 scopes (endoscopies/colonoscopies) on people with autism.

Whether GI problems are more common in children with autism than the general population is not certain, Buie said. However, based on the frequency of gastro problems that he has verified among his autistic patients, Buie said he believes that a thorough GI history and workup should be a part of every person's medical assessment who has autism.

Buie is one of a handful of doctors in the world who treat and evaluate large numbers of those with autism who have GI problems. This is why referred patients can wait up to a year for an appointment with him.

Buie speculates that one reason for the reluctance of other gastroenterologists to treat people with autism is the current medical view that autism is a neurologically based disorder. This view has limited treatment solutions, primarily to behavior therapies.

In addition, people with autism present differently from the general population because they are different, Buie said. This makes diagnoses of GI problems challenging for doctors who are not familiar with these differences. For example, a child with autism who has language deficits may not be able to communicate pain in the same way that a typical child can. Often, a child with autism who cannot talk will communicate pain by actions that are misinterpreted as behavior problems. Many people Buie has treated do not even present strong symptoms of a GI condition. The heterogeneity, or diversity, of autism also complicates a physician's ability to diagnose GI problems.

Also significant is that the treatment of autism has been shrouded by controversy. Speculation

about vaccines causing colitis and autism, and the potential benefit of secretin (used as a testing tool in some children undergoing GI workup) has sent many parents of children with autism to see gastroenterologists who could not answer whether these issues were valid. Dietary and nutritional questions often are raised, but limited research into the value of diet change or use of supplements has made GI and nutrition counseling difficult.

Warning Signs

At MGH, Buie works at one of the leading autism clinics in the United States, the Learning and Developmental Disabilities Evaluation and Rehabilitation Services program, headed by neurologist Margaret Bauman, M.D. Based on their collective experiences, they have developed several "warning signs" that, if seen in a patient, warrant a GI evaluation. Some of these signs include:

1) chronic diarrhea or constipation
2) feeding/eating disorders
3) change in sleep patterns
4) food allergies or apparent changes with particular food exposure
5) behavior changes, especially self-injurious, aggressive or mouthing behaviors

Buie also is a founding member of the GI research group of the Autism Treatment Network (ATN). ATN is a collaboration of leading university hospitals that was formed to address the gap in providing comprehensive medical evaluation and treatment for people with autism, as well as the lack of evidence needed to define a high standard of medical care for people with autism.

Historical Perspective: Dietary Problems

The recognition of dietary problems in people with autism traces back to the original diagnoses of autism by Leo Kanner in1943. In his seminal paper describing autism, Kanner reported that six of his first 11 autistic patients had "feeding or dietary issues."

Since the 1950s, researchers have looked for dietary culprits as triggers for autism. In 1951, researchers D.G. Prugh, Padget Danes and C. Hans Asperger, in separate reports described abnormal, autistic-like behaviors in children with gluten sensitivities.

William Crook, in 1961, found that profound neurological behaviors, including autism and schizophrenia, resolved with elimination of certain foods in selected patients. F.C. Dohan, in 1966, correlated increased cereal and processed grains since World War II with an increased incidence of schizophrenia and autism.

In a 1971 study, Barry Goodwin reported that seven of the 15 autistic children he had randomly selected from a local community for his study had chronic diarrhea. He found that placing these children on a gluten-free diet improved GI symptoms, as well as abnormal EEG findings.

Paul Shattock reported in 1990, and K.L. Reichelt in 1991, that peptides from milk and gluten were found in the urine of people with schizophrenia and autism. They speculated that these products might have contributed to the cause of these conditions.

More recently, S. Lucarelli reported in 1995 that 36 percent of children with autism who were undergoing endoscopy for GI symptoms had allergies. In 1999, K. Horvath found a high incidence of lactose and sugar intolerance among his autistic research subjects. In 2002, he also reported that up to 50 percent of the families he surveyed indicated that their autistic children had food allergies or sensitivities.

Buie's own 2005 study with Rafail Kushak, Harland Winter and Nathan Farber showed that 59 percent of autistic children who were undergoing endoscopy for GI symptoms had carbohydrate digestive abnormalities, compared with only 11 percent in unaffected children undergoing endoscopy for GI symptoms. In this study, duodenal (beginning of small intestine) biopsies were taken from 307 autistic children and 206 non-autistic children selected for endoscopy based on a suspicion of GI problems. Results of the study showed that the frequency of lactase deficiency was higher in autistic children over five years of age than unaffected children, but the frequency was quite high even in the unaffected children with GI symptoms.

Other Important Studies

In a 1998 study, Andrew Wakefield identified lymphoid nodular hyperplasia in the distal ileum (part of the bowel) in seven out of 12 patients with autism, and found that 11 of the 12 patients had frank colitis (a form of inflammatory bowel disease). Buie points out that because of conflict-of-interest charges regarding this work, most of the other authors of this study retracted their support; however, they did not dispute the science behind the study.

Wakefield also published a study in 2000 describing "autistic enterocolitis" as a unique intestinal lesion with prominent lymphoid nodular hyperplasia and colitis. He proposed the MMR vaccine (a three-part vaccine given to protect against measles, mumps and rubella, or German measles) as the cause of the GI pathology. He also hypothesized that increased GI permeability allowed opioid peptides to cause neurological dysfunction or encephalopathic type issues. Buie said that epidemiology studies have disputed a link between MMR and autism, but to date, there have not been independent endoscopic studies evaluating findings and presence of measles virus in the tissue.

In a recent study, Buie's research team found gastroesophageal reflux disease (GERD) and/or esophagitis in nine autistic children who had presented with limited GI symptoms and behaviors not previously associated with gastroesophageal reflux. Buie said GERD is a common condition in pediatrics and should be considered in children with autism. He suggests that GERD

in children with autism may present as behavioral alterations, including aggression or self-injury, and that these behaviors should prompt consideration of underlying pain. Bravo™ pH testing (which involves testing with a capsule that collects pH data and transmits it via radio frequency to a small external pager-sized receiver worn by the patient) may allow evaluation of children who could not tolerate standard pH probe testing, he said. Buie also suggests that population-based data is needed to determine the prevalence of GERD in autism.

R.I. Furlano in 2001, F. Torrente in 2002 and Paul Ashwood in 2004 discussed immune abnormalities and abnormal cytokine profiles (compounds critical to the functioning of immune responses) in children with autism who have GI issues. Buie said he believes that current research regarding GI problems in the autistic population has not yet caught up with the realities of the problems.

Buie said the pitfalls of current autism/GI research are that:

- most of the studies are anecdotal
- there remains an absence of population-based information
- current claims of high prevalence of GI problems in autism remain uncorroborated by mainstream researchers
- much of the current research attempts to offer GI issues as causal rather than contributory to autism symptoms

A Different Perspective

Buie suggests that adopting a different perspective on autism would enhance future research initiatives. The new view would be based on these principles:

- medical issues, including GI disorders, exacerbate autistic behaviors
- recognition and treatment of underlying medical conditions will improve functional outcomes
- raising awareness of underlying medical issues among medical providers will improve quality of life

AUTHORS

Tim Buie, M.D., is a pediatric gastroenterologist at Massachusetts General Hospital for Children and LADDERS, an instructor at Harvard Medical School and assistant clinical professor in pediatrics Tufts School of Medicine. He is also on the medical committee of the Autism Treatment Network.

Kulani Mahikoa is a freelance writer who lives in Portland, Ore.

Evidence for Metabolic Imbalance and Oxidative Stress *in Autism*

BY S. JILL JAMES, PH.D.

It is well accepted that both genetic and environmental factors interact in the development of autism. The search for these factors, however, is proving challenging, with researchers reporting little or no success in replicating findings.

The metabolic aspects of autism have received much less research attention, despite the fact that chronic biochemical imbalance often plays a primary role in the development of complex disease. The metabolism of an individual — that is, the sum of the biochemical reactions in our cells that produce energy and form the materials we need to survive — is affected by both genetic and environmental factors. As such, it gives us a window through which we can view the interactive impact of genes and the environment, and identify relevant susceptibility factors.

Two metabolic impairments of particular interest, because of their association with many neurological disorders, are:

- **Abnormal methylation.** Methylation is a chemical process in which genes are "turned on" or "turned off," and alterations in methylation affect all bodily processes including neurologic and immune function.
- **Abnormal glutathione metabolism.** Glutathione is a crucial antioxidant — a substance needed to protect the body against the effects of heavy metals and other toxins. A deficit of glutathione leads to oxidative stress, in which rogue molecules called "free radicals" damage cells. Excessive free radical damage can lead to abnormal development and function of brain cells, gut mucosal cells and immune cells, which are often impaired in autistic children.

Despite their likely role in neurologic disorders, these processes and variations in the genes associated with them have not been evaluated in autistic children until recently. For the last several years, our Metabolic Genomics Laboratory at the Arkansas Children's Hospital Research Institute in Little Rock has focused on autism. We are discovering that many children with autism have a severely abnormal metabolic profile, indicating significant deficits in cellular antioxidant and methylation capacity.

The best index of methylation capacity is the ratio of two substances, S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH). (This is called the SAM/SAH ratio.) When we tested 95 autistic children and 75 age-matched control children, we found that the autistic children's SAM/SAH ratio was about 50 percent that of unaffected control children (James et al., 2006). In addition, many autistic children exhibited a threefold reduction in the ratio of "active" glutathione (GSH) to "inactive" glutathione (GSSG). Cysteine, another substance needed for GSH synthesis, was also significantly reduced, suggesting that the building blocks for GSH synthesis may be insufficient.

These new findings are of concern because they indicate a significant decrease in cellular methylation capacity and antioxidant defense, and an increase in oxidative stress that could contribute to the pathophysiology of autism. An imbalance in intracellular levels of GSH and GSSG could provide a biochemical explanation for multiple systemic issues, such as increased frequency of infections, gastrointestinal pathology, impaired detoxification and neurologic pathology, that have been associated with both autism and glutathione depletion.

The abnormal metabolite levels in pathways of methionine and glutathione metabolism observed in autistic children may reflect subtle changes in gene products that regulate activity in these pathways. Even small variations in gene expression and enzyme activity, if expressed chronically, could have a significant impact on downstream metabolism.

It is generally accepted that complex diseases such as autism are influenced by genetic alterations at multiple and variable sites that interact to reach a threshold of toxicity that triggers disease expression. We hypothesize that subtle alterations in gene expression may interact with environmental factors to negatively affect pathways of methionine and glutathione synthesis in autistic children. The resulting metabolic imbalance would promote chronic oxidative stress and impaired methylation capacity, and could impair normal developmental maturation of neurologic and immunologic systems.

"Even small variations in gene expression and enzyme activity, if expressed chronically, could have a significant impact on downstream metabolism."

We have used the abnormal metabolic profile of children with autism to guide us in investigating genes that may confer susceptibility to the disorder. The genetic evaluation of an entire metabolic pathway, as opposed to isolated single gene products, provides greater insights into disease pathology and can identify new options for targeted treatment strategies. To this end, our research team has evaluated multiple gene polymorphisms in 360 autistic children and 205 control subjects.

In this relatively small group of children, the results have been surprising and encouraging. Although definitive results will require a much larger study population, we found significant increases in the frequency of genetic changes (polymorphisms) that directly or indirectly affect these metabolic pathways, as well as significant gene-gene interactions (James et al., 2006). Based on these results, we hypothesize that an increased vulnerability to oxidative stress (genetic and/or environmental) and abnormal DNA methylation may contribute to the development and clinical manifestations of autism.

Taken together, our results provide strong evidence that autistic children may constitute a genetically sensitive subpopulation of children who are less able to detoxify environmental exposures. The hypothesis that a genetic component of autism could involve multiple susceptibility gene variants that interact to create a fragile, environmentally sensitive metabolic imbalance is worthy of further pursuit.

Support for a genetically based vulnerability to oxidative stress comes from recent cell culture experiments in our laboratory using lymphoblastoid cell lines derived from autistic children and unaffected controls. We measured the rate of intracellular free radical generation at baseline and found that the autistic cells consistently exhibited higher levels of free radicals compared to the control cells. The addition of nanomolar concentrations of thimerosal to the cells resulted in greater free radical production and induced a greater decrease in glutathione in autistic compared to control cells. Because the autistic and control cells were cultured under identical conditions, these results strongly suggest that the differences observed are due to inherent genetic or epigenetic differences. (Epigenetic changes are heritable changes in gene expression that have several causes, one of which is altered methylation.)

Because abnormal behavior is the most conspicuous manifestation of autism, most current research efforts logically focus on brain pathology. The possibility that the behavioral manifestations of autism may derive in some cases from a genetically based metabolic derangement — one that indirectly affects the brain, immune system and gut — is a plausible but relatively unexplored hypothesis for the biologic basis of autism.

Recent evidence from our laboratory provides support for this broader view that autism involves a systemwide metabolic imbalance that could negatively affect cell function as well as prenatal and postnatal development. If proven correct, this model supports the possibility that normalizing the metabolic imbalance with targeted intervention strategies could potentially improve symptoms and arrest the progression of autism.

"...our results provide strong evidence that autistic children may constitute a genetically sensitive subpopulation of children who are less able to detoxify environmental exposures."

AUTHOR

S. Jill James, Ph.D., is a professor in the Department of Pediatrics at the University of Arkansas for Medical Sciences and the director of the Metabolic Genomics Laboratory at the Arkansas Children's Hospital Research Institute. She received her B.S. degree from Mills College, and her Ph.D. degree in Nutritional Biochemistry from UCLA. Her research career has been devoted to defining gene-nutrient interactions that increase susceptibility to cancer, Down syndrome, birth defects, and most recently, autism. She has published over 100 peer-reviewed papers and recently received the American Society for Nutritional Sciences award for innovative research contributing to the understanding of human nutrition. She is currently funded by a 5 year NIH grant entitled "Metabolic biomarkers of autism: predictive potential and genetic susceptibility."

Environmental Mercury Release
and its Association with Changing Autism Rates

BY RAYMOND F. PALMER, PH.D., AND STEPHEN BLANCHARD, PH.D.

Mercury is a well-defined neurotoxin and now widespread in the environment (EPA, 1997). Next to arsenic and lead, mercury is the third most frequently found toxic substance in U.S. waste facilities (ATSDR, 2001).

While the long-range atmospheric transport of mercury (Ebinghaus et al., 2001) and its conversion to toxic forms through bio-accumulation in the aquatic food chain have been known for some time (Stopford and Goldwater, 1975), more recent concern involves mercury pollution as it effects early childhood development. In a 2000 report, the National Academy of Sciences' National Research Council estimated that each year about 60,000 children may be born in the United States with neurological problems because of exposure to methylmercury in utero.

Body burdens of mercury accumulation can be a result of exposure to a wide range of environmental sources, such as industrial emissions, occupational exposures, dental amalgams, fish consumption (EPA, 1997), or through mercury-based preservatives used in some vaccines (Freed et al., 2002). The largest source of potential population exposure comes from coal-fired utility plants, municipal/medical waste incinerators, and commercial/industrial boilers—estimated to be responsible for 158 tons of environmental release per year in the United States (EPA, report to Congress, 1997).

Other sources include hazardous waste sites, cement factories and chlorine plants. While the acute neurotoxicity of mercury is well known (ATSDR, 2001), population risks associated with low-level persistent exposure are poorly understood (NAS, 2000); yet reports implicate mercury in the causation of various developmental and learning disabilities (Ramirez et al., 2003), including autism (Bernard et al., 2001, 2002; Vojdani et. al., 2003).

Environmental Mercury Investigations

We have investigated the hypothesis that environmental mercury may be associated with population autism rates. Our preliminary investigation was initiated by noting that changes in autism over time corresponded with geographic regions where mercury and other toxic environmental releases were at the greatest level.

The top portion of Figure 1 shows the geographic trends in autism over approximately 10 years in Texas. The bottom portion depicts a geographic correspondence of environmental toxic release. The bottom right panel of Figure 1 shows that counties with the greatest rate of change in autism are either counties with the highest levels of toxic releases or those that border counties with the highest levels. There are some notable exceptions. One is Brewster County (the large county bordering Mexico in the west, with the dark border representing a rapid increase in autism but no reported toxic release). Interestingly, the economic history of this county includes being the leading producer of mercury in the United States.

Our recently published study demonstrates an association between environmental mercury release and autism in Texas. We found that for every 100 pounds of environmentally released mercury there was an associated six percent increase in the rate of autism (Palmer et al., 2006). Critics have argued that "exposure" was ill defined, and that distance to exposure sources would have been a better proxy for population exposure. Further, causal inference was limited because the study was cross-sectional and ecological rather than individual in nature.

To address some of these concerns, we conducted a second study in which we demonstrated that distance to industrial sources of mercury was inversely related to changes in the rate of autism over the last 15 years. These findings are consistent with existing research studies conducted with soil and plants (Wang and Shi, 2003; Kalac, 1991), and humans (Kurttio et al., 1998; Horvat, 2003), which demonstrate that proximity to mercury sources is related to greater burdens of mercury.

In a recent analysis, we used data from the U.S. Environmental Protection Agency's National Air Toxics Assessment (US EPA NATA) of 1996, based on a comprehensive analysis of mercury emissions obtained from various state and local air pollution control agencies. Associating this data with statewide-level autism data obtained from the "U.S. Department of Education Office 25th Report to Congress," we show that autism rates among children three-to-five years old in 2000 (e.g., those children conceived or born between 1995 and 1997) were significantly higher among states with greater concentrations of ambient air mercury per square mile. Figure 2 depicts this association.

Ambient air mercury was found to explain 20 percent of state-level autism rates. This association remains significant after adjusting for relevant factors, including baseline levels of autism, percentage of state spending for education and number of pediatricians.

Consistent with our results, Windham et al., (2006) demonstrate that mercury in the air is related to increased risk of autism. Compared to families living in areas of lower air concentrations of mercury, the researchers found that families living in higher-concentration areas were significantly more likely to have autistic children.

Taken together, these studies offer important justification

for further investigations. While our studies demonstrate a positive association between environmental mercury release and autism, they are preliminary because it is potentially erroneous to draw conclusions about individual risk from population-based ecological studies such as ours. These studies serve as the first phase of a larger study initiative involving the connection between environmental neurotoxins and autism.

We currently are pursuing studies that will involve understanding the interaction between genetic susceptibility and amounts of toxic environmental exposures. We suspect that persistent environmental toxic exposures in the presence of a genetic predisposition for poor detoxification of neurotoxins will put individuals at risk for developing autism. Knowing the specific combinations of environmental exposures and genetic predispositions can inform the development of targeted intervention strategies geared toward preventing autism.

AUTHORS

Raymond F. Palmer, Ph.D., is associate professor for the department of family and community medicine at the University of Texas Health Science Center in San Antonio.

Stephen Blanchard, Ph.D., is professor and chair of the department of sociology at Our Lady of the Lake University, also in San Antonio.

REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR), 2001. CERCLA Priority List of Hazardous Substances. U.S. Department of Health and Human Services, Public Health Service, Atlanta. www.atsdr.cdc.gov/clist.html.

Bernard, S., Enayati, A., Redwood, L., Roger, H., Binstock, T., 2001. Autism: a novel form of mercury poisoning. Medical Hypotheses 56, 462–471.

Bernard, S., Enayati, A., Roger, H., Binstock, T., Redwood, L., 2002. The role of mercury in the pathogenesis of autism. Molecular Psychiatry 7, S42–S43.

Environmental Protection Agency, 1997 Mercury Study Report to Congress. Publication number: EPA 452/R97-003

Ebinghaus, R; Kock H., Schmolke S. Measurements of atmospheric mercury with high time resolution: Recent applications in environmental research and monitoring Fresenius J Anal Chem 371 :806–815. 2001

Freed GL, Andreae MC, Cowan AE, Katz SL. The process of public policy formulation: the case of thimerosal in vaccines. Pediatrics. 2002;109:1153–1159

Horvat M. Nolde N. Fajon V. Jereb V. Logar M. Lojen S. Jacimovic R. Falnoga I. Liya Q. Faganeli J. Drobne D. Total mercury, methylmercury and selenium in mercury polluted areas in the province Guizhou, China. Science of the Total Environment. 304(1-3):231-56, 2003

Kalac P. Burda J. Staskova I. Concentrations of lead, cadmium, mercury and copper in mushrooms in the vicinity of a lead smelter. Science of the Total Environment. 1991,105:109-19.

Kurttio, P. et al., Increased Mercury Exposure in Inhabitants Living in the Vicinity of a Hazardous Waste Incinerator: A 10-Year Follow-up. Archives of Environmental Health. 1998, 53(2):129-137

National Academy of Sciences (NAS), 2000. Toxicological Effects of Methylmercury. National Academy Press, Washington, D.C.

Palmer RF, Blanchard S, Stein Z, Mandell D, Miller C. Environmental Mercury Release, Special Education Rates, and Autism Disorder: An Ecological Study of Texas. Health and Place, 2006, v12: 203-209.

Ramirez, G., Pagulayan, O., Akagi, H., et al., 2003. Tagum study II: follow-up study at two years of age after prenatal exposure to mercury. Pediatrics 111 (3), e289–e295.

Stopford W. and Goldwater L. Methylmercury in the environment: A review of current understanding V 12. p115-118. 1975

United States Department of Education. Twenty-Fifth Annual Report to Congress on the Implementation of the Individuals With Disabilities Education Act. Jessup, Md: Bureau of Special Education; 2003.

United States Environmental Protection Agency, 2006 (US EPA NATA). http://www.epa.gov/ttn/atw/nata accessed 6/^7/2006.

Vojdani A, Pangborn JB, Vojdani E, Cooper EL. Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism. Int J Immunopathol Pharmacol. 2003;16(3):189-199

Wang D. Shi X. Wei S. Accumulation and transformation of atmospheric mercury in soil. Science of the Total Environment. 304(1-3):209-14, 2003 Mar 20.

Windham GC, Zhang L, Gunier R, Croen LA, and Grether JK. 2006. Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the San Francisco Bay Area Environ Health Perspect:doi:10.1289/ehp.9120. [Online 21 June 2006] http://ehp.niehs.nih.gov/docs/2006/9120/abstract.html

As a member of the Autism Society of America, Comfy Sack will be donating $15 from each order to ASA's Online Giving Campaign when the promotion code 'HelpAutism' is used.

The Comfy Way to Giving

Comfy Sacks

www.ComfySacks.com

USE CODE: HELPAUTISM

Give A Special Holiday Gift to the One You Love!

"Our son Casey loves his new Comfy Sack. It is a great piece of furniture that relaxes our Autistic son. In fact the very first night we had it, he slept on it! Now that's comfort.

-Cheri and Kevin O'Day - Indianapolis, IN
Educators and Parents of Casey O'Day

As more and more customers purchase our comfortable soft chairs, we are flooded with positive feedback from enthusiastic parents touting the benefits that their disabled children received from the Comfy Sack. They are the softest foam bag chairs on the market and are able to meet the sensory needs of children with Autism by creating a feeling of safety, security, and comfort far superior than that of a normal bean bag chair.

The Comfy Sack will become your child's favorite place to enjoy time with you. Whether it's learning time with flash cards, reading together, or fun time with television or video games....a Comfy Sack will make your time with your child more special.

Our favorite fabric by far is micro suede. It is the best available and is often compared to the feel of falling into a cloud as you sink into it's softness. Comfy Sacks offer the highest quality foam and fabric (complete with it's own liner) for half the price of other similar products sold in malls.

www.ComfySacks.com

Why Time Trends in Autism Matter

BY MARK F. BLAXILL

Few now question the high rates of autism reported in the United States, estimated anywhere from one in 175 to one in 166. However, the question of whether these high rates represent a *rapid, real increase* in the incidence of autism is surprisingly controversial.

Influential observers such as Harvey Fineberg, president of the Institute of Medicine, have asserted, "It's…clear that the definition [of autism] was broadened markedly in the 1980s and 1990s, and there were increased incentives to recognize children from increased awareness and availability of services. No one knows with certainty what part of the increase is genuine, a genuine increase in numbers, and what part is from increased recognition of people who were already there but not previously recognized."

For those of us who live with a child with autism, the notion that just two decades ago we might have missed the diagnosis of something like 90 percent of affected children seems to hardly merit serious discussion.

However, surprisingly few scientists, epidemiologists and public health officials have questioned the claims of major figures such as Fineberg. Many take the attitude that since we cannot perform the ideal studies to measure autism trends retrospectively, we can never know the true answer to the question of whether autism rates have gone up. Along with this attitude goes a lack of urgency and a presumption that the answer to this question has little importance. This line of thinking further begs the most basic questions of epidemiology: What can the specific location (in space and time) of the autism epidemic teach us about its roots?

On the question of time trends, I will offer this assertion: There can be little doubt at this point that real rates have risen sharply. Explaining away a tenfold increase requires proof of a hypothesis of large-scale diagnostic error. This is a simple and testable hypothesis. Numerous tests of the diagnostic error hypothesis are available, and the theory of large-scale error fails every test. In plain terms, the theory is false; the epidemic is real.

Why does this matter? With respect to the strategic direction of autism science, I submit that the most important question is that of time trends.

To make this point more specific, consider for a moment the resource implications of four positions regarding time trends:

1. "We don't know" if the increases are real or if there is just greater awareness of the disorder and better diagnosis. As long as doubt about time trends persists, so does the case for the *status quo* in the management of autism science. Given this view, major changes in the direction and amount of funding can be reasonably deferred.

2. "It doesn't matter" whether rates are going up—it's enough to recognize that they are high. Treating the recent high autism rates as a kind of discovery, a surprising but otherwise unremarkable bit of health news, permits research planners to embrace a higher priority for autism spending without resolving the hard questions that the time trends raise. If rates truly have gone up, then how should we judge the decision to allocate millions of research dollars based on the assumption that autism is a rare, genetically driven disorder? Obviously, we should view it as a flawed plan. This second position, therefore, encourages ongoing reward for unproductive science.

3. "Let's rule out" certain inconvenient environmental hypotheses, such as vaccines and their preservatives. The timing of the sharp increases in autism rates offers important clues regarding the pathogenic processes underlying neurological development in otherwise typical children. Yet this third position, which imposes arbitrary and selective placement of restrictions on the scope of environmental research, places blinders on scientists at a time when we can little afford the luxury of selective ignorance. When we need environmental science to proceed with the maximum degree of flexibility, this position suggests we restrict research into plausible (and scientifically supported) environmental agents such as mercury and childhood vaccines simply because, if implicated more fully in pathogenesis, that knowledge raises uncomfortable implications.

4. "We have a crisis" and, therefore, we must treat the investigation into the environmental causes of autism rates as a national public health emergency. The only rationally defensible position, when one confronts the fact and the timing of the increased rates of autism, is to recognize that we are in an emergency situation. Emergencies greatly simplify decision rules, require the removal of resource constraints, require clear strategies and creative exploration of solutions, require a suspension of the assignment of blame until causation can be established, and eventually require the assignment of accountability and the extraction of lessons for the future. But does this position guide the strategic governance of autism science today? Unfortunately, it does not.

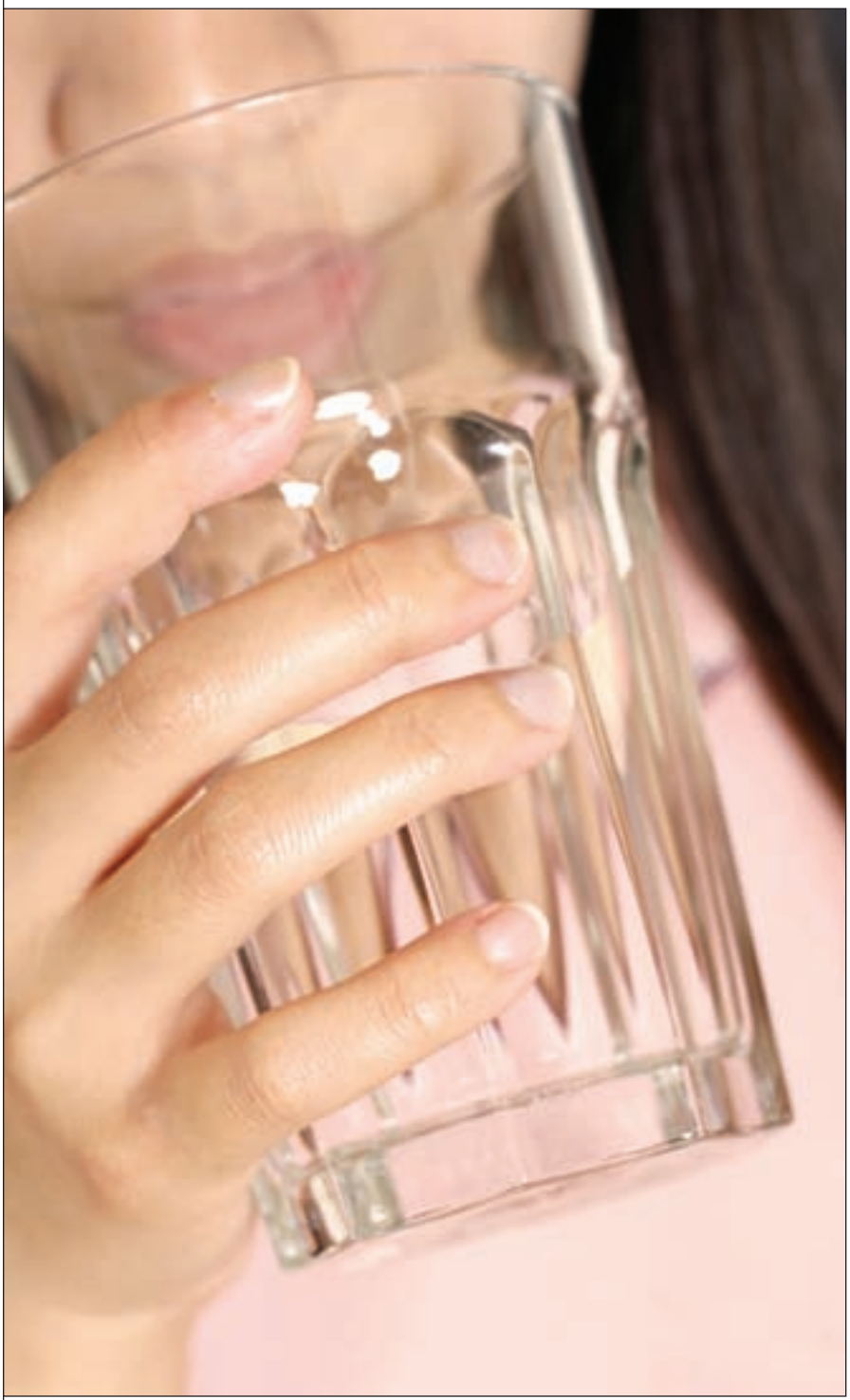
Until we come to grips with the question of time trends, autism science will perform poorly. We cannot afford to wait.

AUTHOR

Mark F. Blaxill is vice president of SafeMinds.

Transforming the Public Debate on Neurotoxicants: *The Learning and Developmental Disabilities Initiative*

BY ELISE MILLER, M.ED.



© SUPRIJONO

Learning and developmental disabilities (LDDs) appear to be on the rise, affecting at least 17 percent of youth in the United States under the age of 18.[1] Though there is some controversy about how new diagnostic tools may be contributing to these increasing statistics, one in six of our children struggling with these issues is simply too many.

A number of factors—heredity, gene expression, social environment, nutrition and synthetic chemicals—contribute to brain development in complex ways. Recent research, however, reveals that exposures to certain neurotoxicants, such as lead, mercury, pesticides, polychlorinated biphenyls (PCBs), polybrominated diphenylethers (PBDEs) and some solvents can have a particularly detrimental impact on brain function and in turn lead to the expression of learning and developmental disabilities.[2] These environmental contributors often are the least researched and ultimately the most preventable.

We also know from research that developing fetuses and children are more vulnerable than adults to environmental exposures for a variety of reasons. For example: their biological systems are still developing; they metabolize at a much faster rate; pound per pound, they eat, drink and breathe far more than adults; and their behavior, such as crawling on the ground and putting their hands in their mouths after touching the floor, results in higher exposures to toxins. If they are exposed to even low doses of toxic chemicals at critical windows of development, their ability to achieve their full potential may be impaired for life.[3]

The Learning and Developmental Disabilities Initiative: Preventing Exposures to Neurotoxicants

To date, most learning and developmental disability groups have focused on identifying affected children and getting them the services they need—something that is, of course, very important. However, there is a parallel need for prevention of exposures that lead to these disabilities in the first place. Under the auspices of the Collaborative on Health and the Environment (CHE), the Learning and Developmental Disabilities Initiative (LDDI) was formed in 2002 to engage national and regional learning and developmental disabilities groups interested in looking upstream and focusing on the prevention of exposures to neurotoxicants.

At the first meeting of LDDI in May 2002 in Washington, D.C., the group determined that the national LDD sector, with its hundreds of thousands of members, in collaboration with scientists and key environmental health and justice organizations, could be an effective voice for protecting children from toxic hazards related to altered brain development. Participants adopted LDDI's mission: to foster collaboration among learning and developmental disability organizations, researchers, health professionals and environmental health and justice groups to address concerns about the impact environmental pollutants may have on neurological development.

LDDI has almost 250 organizational and individual members engaged in research, educational and policy efforts. The Learning Disabilities Association of America (LDA) was the first organization to develop a model program focusing on protecting children from neurotoxicants, having already begun to look at toxic contributors to learning disabilities over the past several years. As an extension of their engagement with LDDI, the LDA has established a new national Healthy Children's Project, with initial focus in state chapters in California, Maine and New York. Since then, 16 additional state chapters have undertaken environmental health projects.

The American Association on Mental Retardation (AAMR), which published a report more than 20 years ago on environmental links to mental retardation, has reinvigorated its interest in the impact toxic exposures may have on brain development. Working with colleagues in LDDI, AAMR organized a conference on "pollution, toxics and mental retardation" in July 2003. This was the first national meeting to bring together the developmental disabilities and environmental health sectors to discuss national educational and policy-oriented strategies regarding neurotoxicants and developmental disabilities. Since then AAMR has initiated extensive educational and policy efforts nationally among its members.

With LDDI encouragement, the Autism Society of America (ASA) has been the third major national LDD organization to establish an environmental health program. It is clear, given ASA's respected leadership in regard to autism and autism spectrum disorders, that this action will help transform the attitudes of professionals in the developmental disabilities field regarding the effects of toxins on neurodevelopment.

In addition to these groups, LDDI is working with the Arc of the United States, the National Association for the Dually Diagnosed, SafeMinds, YAI/National Institute for People with Disabilities, and Communities Against Violence Network, as well as many other academic, health professional and advocacy organizations. Among their many efforts, LDDI members have published summaries on neurotoxicants found in human blood and urine samples as reported by the Centers for Disease Control, organized a congressional briefing, drafted letters to the U.S. Environmental Protection Agency about specific neurotoxicants, made presentations at major national professional meetings, and published 11 "Practice Prevention" columns that highlight how lay people can protect their children and themselves at home from neurotoxicants. (www.iceh.org/LDDI.html)

LDDI will hold its second major national meeting for researchers, health professionals, LDD organizations and environmental health advocates at the Morehouse School of Medicine in Atlanta, Ga., May 10-11, 2007. This conference will expand on LDDI's central focus on neurotoxicants and include other factors, such as nutritional and socioeconomic concerns, in relation to healthy neurological development.

Overall, the organizations involved in LDDI have well over 500,000 members combined—a significant sector of our society with a powerful voice to create positive change. With the increased knowledge about environmental concerns obtained through their association with LDDI, these groups and individuals will have the opportunity not only to make healthier choices personally, but also to press for appropriate policies that protect children from toxic exposures so that they can lead full and healthy lives.

AUTHOR

Elise Miller, M.Ed., is founder and executive director of the Institute for Children's Environmental Health and the national coordinator for the Collaborative on Health and the Environment's Learning and Developmental Disabilities Initiative (www.iceh.org/LDDI.html). She also is a member of the ASA Environmental Health Advisory Board to defining gene-nutrient interactions that increase susceptibility to cancer, Down syndrome, birth defects, and most recently, autism. She has published over 100 peer-reviewed papers and recently received the American Society for Nutritional Sciences award for innovative research contributing to the understanding of human nutrition. She is currently funded by a 5 year NIH grant entitled "Metabolic biomarkers of autism: predictive potential and genetic susceptibility."

Requirements for Good Scientific Inquiry

BY G. JEAN HARRY, PH.D.

Scientific inquiry assumes many forms, ranging from anecdotal reports of clinical observations to studies under tight experimental control. They all have a common feature however: They initiate a chain reaction.

Simple observations or case reports frequently become the basis for more systematic and controlled studies. Often, studies raise additional questions concerning the hypothesis being tested, which leads to more research. This iterative process is the basis for the scientific method. Most important, however, is the principle of replication. Others must replicate results from one laboratory or study before they are considered to be valid by other scientists. In this way, the scientific method is self-correcting.

Accumulation of data generated by high-quality studies allows one to evaluate theories based on the principle of hypothesis testing. Generally, theories cannot be proven, only supported by the data available. Research involves testing a hypothesis empirically through experimentation. Data are either consistent with the theory or not, resulting in a reformulation of the theory or the generation of a new one altogether.

Problems of interpretation and meaningfulness of the results can develop when the experiments are designed with a narrow mindset that does not allow for evaluation of competing theories or for generating data that might be contrary to established dogma. Unless precautions are taken in the experimental design, unintentional bias may be introduced into the studies. This can lead to erroneous, and often costly, assumptions and conclusions.

It is crucially important in the evaluation of data from studies that may impact public health policy that the reader understands the scientific method. One must consider 1) the ultimate impact and use of the results, 2) the validity of the test methods, 3) the reliability of the data, 4) the biological plausibility of the results and 5) the degree to which the data can be applied from the narrow conditions of the study to "real world" conditions.

It is critically important to realize that the publication of data from a single or limited number of studies does not mean that the conclusions are "true." Data from any given study are only as good as the experimental design and proper execution of methods. As mentioned previously, other investigators must replicate findings before the scientific community will accept results as being valid.

Research and Public Health Issues

Because of the direct relevance to policy and the lives of people, research in the public health arena demands high-quality data and strict standards for conducting studies and reviewing results. Results from inadequately designed and conducted studies might be used to support a course of action that would not be appropriate or would delay consideration of alternatives.

Because most public health issues are broad in scope and likely to span a number of different disciplines, and because emerging complicated technologies and methods may contribute enormously to the design and interpretation of such studies, research on public health issues requires that investigators take on certain responsibilities. It is the responsibility of public health researchers to recognize that studies conducted outside of their own specific expertise could be based on naïve or outdated assumptions or use insensitive or inappropriate methodologies.

Thus, there is a demand and responsibility for setting guidelines for appropriate study design and testing procedures. This need for guidelines is not new. For example, government, academia and industry have all contributed expertise to develop national and international testing guidance documents for conducting appropriately designed studies to assess various forms of toxicity and treatment efficacy.

These guidance documents clearly lay out the need for relevant scientific expertise, valid tests and study replication, and experimental design and data handling. They are a major source of information for anyone undertaking similar studies and reinforce the need for identifying good test methods. Such principles need to be applied seriously in studies involving assessments of how environmental factors may affect public health.

It is the responsibility of both the researcher and the public to demand the highest standards for the design, conduct, data analysis and interpretation of studies that may influence public health policy. A critical and skeptical approach to all public health findings should be encouraged, and efforts to validate and reproduce critical findings having public health policy implications should be supported. It is critical that we appreciate both the scientific method and the complex nature of most public health questions, so that we stay open to all possibilities and to alternative hypotheses that may emerge.

AUTHOR

G. Jean Harry, Ph.D., is head of Neurotoxicology Group, Laboratory of Neurobiology, National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services Research in Triangle Park, N.C.

The 'Three Strikes' Concept of Autism

INTERVIEWED BY JUDY CHINITZ GORMAN; EDITED BY DR. IAN LIPKIN AND DR. MADY HORNIG

Since the 1980s, Dr. Ian Lipkin has investigated the links between infection, immunity and brain disorders. In 1995, Dr. Mady Hornig introduced him to screenwriter and Emmy Award-winning art director, Portia Iversen and her husband, movie producer Jonathan Shestack, the founders of CAN (Cure Autism Now).

Impressed by their dedication, and concerned with the overall lack of awareness of the significance of this public health problem, Lipkin became an advocate for autism research. As the first chair of the scientific advisory board of CAN, he recruited a distinguished group of neuroscientists and physicians, and helped develop grant mechanisms to bring new investigators to the field. He also began to shift his laboratory's efforts to autism research.

Hornig's investigations into the importance of brain-immune interactions in the development of neuropsychiatric illness also date back to the early 1980s with work on the combined modulation of brain function by immune and central nervous system factors. Intrigued by the concept that the immune system often is responsive to environmental stressors, she hypothesized that variations in the individual's genes and maturational state, combined with these stressors, were important to health outcomes.

Lipkin and Hornig use animal models and epidemiologic approaches to dissect potential causes of neurodevelopmental disorders and to test potential strategies for early diagnosis, prevention and treatment. Their work has led to the "three strikes" concept of neurodevelopmental disorders such as autism, whereby genetic susceptibility (strike one), environmental triggers (strike two) and the timing of exposure during periods of vulnerability for the developing nervous system (strike three) result in disease. This concept integrates genetics, microbiology, developmental biology and toxicology, and explains why efforts that focus on only one of these disciplines have not been successful.

After demonstrating the biological plausibility of the three strikes paradigm in animal models of neurodevelopmental disorders involving infection, autoimmunity and toxicant exposure, Lipkin and Hornig began to search for ways to explore the three strikes principle in children. A unique opportunity to do so emerged in 2000 when they were invited to join the faculty of the Mailman School of Public Health by Dr. Ezra Susser, a pioneer in birth cohort research. In conjunction with the Norwegian Institute of Public Health, the team began a unique autism research initiative, the ABC Project: Gene-environment Interactions in an Autism Birth Cohort (www.abc.columbia.edu).

The ABC project involves collecting 100,000 samples of umbilical cord blood from a random population of Norwegian infants, along with biological samples from their mothers, beginning at the 17th week of pregnancy. Samples also are taken from their fathers. By following the infants' natural histories over years, recording physical and behavioral anomalies, rigorously diagnosing and characterizing a subset of autism cases and controls, and comparing their genetic materials, the team has an excellent opportunity to identify both the biomedical markers that may make children susceptible to autism and the environmental factors that may tip the scales: viruses, bacteria, toxins such as mercury or PCBs, psychosocial stress, or combinations thereof.

They can compare the DNA of children who develop autism to those who do not to better understand heritable risks, and measure levels of messenger RNAs and proteins to learn when various genes important for brain development are turned on and off. Identification of specific patterns of gene expression can provide tools for diagnosis at birth and insights into the causes of different subtypes of autism spectrum disorders that may lead to new strategies for prevention or treatment.

Lipkin brings to this program what he describes as a "peace dividend" from his work in biodefense research: exciting new techniques for rapid, sensitive detection of infection and disordered immunity, and high throughput molecular investigations.

In the near future, Lipkin and Hornig, in collaboration with Drs. Margaret Bauman and Timothy Buie, both at Harvard University's Massachusetts General Hospital, will publish research on the relationship of the measles-mumps-rubella vaccine to autism.

AUTHORS

Dr. W. Ian Lipkin is the Jerome L. and Dawn Greene professor of epidemiology, and professor of Neurology and Pathology in the Mailman School of Public Health (MSPH), and College of Physicians and Surgeons at Columbia University in New York.

Dr. Mady Hornig is an associate professor of epidemiology at MSPH and director of translational research in the Greene Laboratory.

Judy Chinitz Gorman is the parent of two sons, one of whom has autism. She holds a master's in special education and is currently pursuing another in nutrition.

THIS IS THE STORY OF A PERSON WITH A BEAUTIFUL SPIRIT AND A LEARNING DISABILITY— WHO DISCOVERED A WAY TO GO TO COLLEGE.

We know people who once thought college wasn't an option for them. In fact, we see them daily, because we're the people who are making sure college is an option. **We're CLE—College Living Experience—and not only do we make college possible by offering an unparalleled network of academic support, we teach independence.** Our students go to college while learning to live on their own. They're making the grade and a home at the same time. **CLE. College made possible.**

CLE
College *Living* Experience

Our students.

Our students are those for whom success, career and independence are possible. Their challenges include:
Learning Disabilities • ADD/ADHD • Psychosocial-Maturational issues • Aspergers • Nonverbal Learning Disorder

Ask about CLE locations in Austin, Denver and Ft. Lauderdale • Call us at **800.486.5058** or visit **cleinc.net.**

Biomedical Treatment of Autism

BY JOHN GREEN, M.D.

©CHRISTINE BALDERAS

I chose a career in medicine, combining my love of the humanities and sciences. In the clinic, I often was more interested in my patient's stories than their symptoms and diagnoses. Medical training under the rigorous aegis of our professors taught us to take care of diseases, but not of our patients or ourselves. Exhausted and frustrated by the training process, I left my family practice residency after one year and took a job in emergency medicine.

I found much satisfaction in the ER, treating acute illnesses and injuries with tools that really helped care for acute human suffering. But after a few years, I recognized the limitation of the acute care model, as my ER shifts became crowded with patients who would call ahead to find out when Dr. Green was on duty so that they could seek help for chronic health problems that were unresolved by their primary care physician.

In 1981, I discovered the Society for Clinical Ecology, now called the American Academy of Environmental Medicine. Clinical ecology brought a whole new set of questions to the diagnostic investigation, such as: What is the patient eating, drinking, breathing, wearing or harboring in his body that is triggering/inciting symptoms and tissue injury, leading to a diagnosis of medical illness?

We also learned to explore the deficiencies, weaknesses or predispositions that increase susceptibility to injury. Using these tools, I found that many people with chronic health problems could be helped immensely. This led me out of emergency medicine and into the care of chronically ill patients. I later found that the principles taught in clinical ecology are the same principles

upon which the Defeat Autism Now! (DAN!) approach to autism diagnosis and treatment is based.

In the mid 1990s, a mother brought her four-year-old son with autism, Jordan, to me for evaluation. He was only the third person with autism I had treated, and at that time, his mother knew more about the disorder and its treatment than I did.

We approached his treatment together, with mom helping me to let go of stereotypes I had acquired about autism as an untreatable illness. She also helped me to access tools that I'd used in investigating many other types of chronic illness (i.e., looking at his biochemistry, allergies, gut flora, toxins and general nutritional adequacy, and supporting the family's strengths).

Jordan made great progress over the years, doing well academically, becoming involved in religious training and demonstrating real talent as a musical performer. Jordan has a few residual deficits—a speech impediment, allergies and mildly concrete thinking—for which he compensates with a delightful sense of humor, a very affectionate nature and a striking concern about justice. Jordan and his mother opened for me the world of treating children with autism.

I began to see a few other affected children, and in 2000, a mother whose daughter with autism had begun to improve under my care brought to me a deluge of children with autism spectrum disorders (ASD). I became acquainted with more parents of children with ASD and was amazed at the devotion, intelligence and commitment that are common to people with autism. The severity of the autism epidemic became palpable to me, and a growing sense of urgency developed. I learned more about caring for the affected children, and felt a growing need to commit my practice to these children and their families. So for the past five years, I have been saying goodbye to my faithful adult patients and accepting only children with ASD into the practice.

"The severity of the autism epidemic became palpable to me, and a growing sense of urgency developed."

Basic Principles about Autism

There are a number of basic principles about autism that must be understood.

1) Autism is not a diagnosis, but rather a classification based on behaviors, which are caused by injury or imbalances. The diagnosis is useful in that it activates parents to seek help, provides a term to use on the Internet for further study, gives access to rehabilitation services, and allows scientists to group children with this diagnosis together for further study and treatment. It would actually be better to talk about "autisms," as children with the same diagnosis are quite different from each other.
2) Symptoms are a language of the body and an indication of distress, such as pain, fear, frustration and a biochemical disruption. While treating symptoms may ease distress, we must always seek to get to the core issues causing the distress. For example, a child's agitation may be better treated by removing an allergic food or clearing an impacted bowel than by giving him Risperdal (an antipsychotic drug).
3) Most children gradually improve in response to effective treatment and in a stepwise or incremental fashion. While there are many stories of dramatic, quick recoveries, these are infrequent. The majority of children improve gradually with much work and with periodic setbacks and readjustments.
4) A child's symptoms result from an overload of demands (allergens, infectious agents, toxins, psychosocial stresses, inflammation, oxidative stress) in combination with weakness or susceptibilities, which impair ability to respond to the demands (impaired energy production, inherited enzyme weakness, nutritional deficiencies, osteopathic disorders, sleep deficits, hormone imbalances, etc.).
5) Each child is biochemically individual, and even identical twins are not an exact match in biochemistry or genetic expression. Stories of other children may prove helpful to the care of your child, but it is most important to focus on your child as a unique person.
6) As Dr. Martha Herbert (see article on page 18) has observed, the brain is connected to the rest of the body, and what happens to the body affects the brain.
7) Grandmother did know best, and cod liver oil really is good for most of us. Nutritional deficiencies/dependencies are rampant in the population and particularly in children on the autism spectrum.
8) There are many self-perpetuating cycles of tissue injury and dysfunction that operate in people with chronic illness such as autism. Breaking these cycles is necessary to help free the body to heal and restore its own physiologic pathways.

   For example, the child born by cesarean section fails to get the normal gulp of vaginal mucus to colonize the GI tract with probiotic flora. Absence of lactobacillus may be associated with increased allergic problems. Allergies in young children frequently lead to infections, with consequent antibiotics. Antibiotics tend to further disrupt intestinal flora and may lead to colonization with pathogenic yeasts and bacteria. These organisms may produce abdominal distress and also neurotoxins, which affect eating behaviors, leading to preferences for simple sugars and less nutritious foods.

In addition, disruption of bowel flora is associated with impaired digestion and assimilation, and also reduced production of essential nutrients such as pantothenic acid, biotin and vitamin K. Many of these issues aggravate the tendency to infections, allergies, further immune disruption and impairments in detoxification systems. Early on, the supplementation of the cesarean section infant with good bacteria may prevent or short-circuit some of the cycles described above and help the child to develop a healthy immune response and a healthy digestive tract.

In more advanced cases, improvement of the quality of the diet, enhancement of digestion and absorption, restoration of normal GI flora and elimination of toxic organisms may contribute to breaking the extensive cycles described above. In fact, if one looks closely at the pathologic findings that are common in autistic children, such as oxidative stress, overload of toxins, chronic inflammation, and impaired energy production and neurotransmitter signaling, each feeds into other negative cycles of illness. Our task in treatment is to identify and break such cycles as thoroughly as possible.

9) The medical treatment of children with ASD has small inherent risks, most commonly of transient setbacks associated with hypersensitivity to an intervention or a chosen treatment method that is off the mark. The risk of serious harm in the hands of a capable trained physician is extremely low. The risk of not treating these sick children and hoping for spontaneous improvements is much greater than any risk of treatment.
10) Early initiation of comprehensive treatment greatly enhances the effectiveness of therapy and the extent of benefits to be expected.
11) There still are significant unanswered questions in autism, but at this point we know enough to expect to help every child with treatment and to see a recovery in many children.
12) Treatments can be tough for parents and require tough love. Remember, while tough love is tough, it is love.

Autism as a Systemic Illness

My evaluations of more than 1,000 children with ASD have demonstrated clearly that these children are physically ill, afflicted with significant problems in many organ systems. The work of treating them amounts to two basic processes, both aiming to restore balance and vigor, and proper communications extending from the cellular level to the interpersonal.

The first basic process is the identification and treatment or removal of obstacles to healthy organ activity. There are many such obstacles in the worlds of children with ASD, some obvious and some subtle. Commonly encountered obstacles include allergies and food intolerances, metal and chemical toxicities, infections (fungal, viral, bacterial, parasitic and mycoplasmal), oxidative stress (problems with electrons moving around in the body out of control), acidosis (too much acid being produced in the system, though usually not in the stomach, where it is needed), and psychosocial stress (sensory issues, confusion and frustration, difficulty recognizing and receiving love, etc.). A child may show major improvement simply by clearing an obstacle that is troubling him, such as a food intolerance, yeast infection or metal poisoning.

The second basic process is identifying what is weak, disrupted or deficient in a child and working to overcome or compensate for the impairment. Among the issues that must be addressed:

"The first basic process is the identification and treatment or removal of obstacles to healthy organ activity."

- ASD children often have impairments or deficiencies in immune defenses (especially in cellular immunity and in the proper regulation of the immune response).
- They are commonly deficient in many essential nutrients due to self-restricted diets, poor digestion and absorption, nutrient wasting through cellular energy disruption or nutrient-depleted food supply.
- Their tissue oxygenation may be disrupted by stiff red blood cells, abnormal clotting tendencies and acidosis. Excess acid in the system results in hyperventilation (over-breathing), which decreases brain blood flow.
- Deficiencies in digestive factors are extremely common, including essential enzymes (dipeptidyl peptidase IV [DPP-IV] and others), stomach acid, intestinal hormones (secretin, cholecystokinin [CCK]), bicarbonate (acid neutralizer), secretory IgA (antibody lining and protecting the mucous membranes) and beneficial flora (friendly germs).
- Neurotransmitter levels and activities often are weak in ASD, related to a number of factors, including malabsorption of essential amino acids, impairment of methylation (dependant on B6, B12, folic acid and magnesium) and oxidative stress.
- Weakness in detoxification functions also is common in ASD. There are many aspects to this problem, salient factors being: impaired synthesis of glutathione (a personal cellular "bodyguard"), disruption of the activity of metallothionein (a super-potent metal chelator made in the body) and depleted sulfation pathways (which can cause impaired detoxification and additional biochemical disruptions).
- Children with ASD often have injuries or imbalances in thyroid and adrenal glands that need attention.

- Finally, these children often have obsessive tendencies and almost addictive behaviors that lead to restrictions of input in many critical areas, including balanced diet, effective play, social learning, problem solving, physical activity, language and positive emotional feedback.

Environmental Factors in Autism

There is increasingly strong evidence that the autism epidemic, along with increases in many other childhood diseases, is related to environmental toxins (in addition to mercury). These toxins are persistent, bioaccumulative agents, which are found in food, water and air.

Some of these harmful agents include PCBs, flame retardants, plastic derivatives, pesticides and herbicides, fluorinated hydrocarbons found in Teflon, and a long list of toxic waste products that are added to fertilizer as a means of disposal. These types of chemicals produce oxidative stress (inability to protect the brain and other sensitive tissues from our own metabolic byproducts), hormone disruption (especially thyroid and sex hormones), obesity and insulin disturbances (arsenic and MSG), and impairments in neurotransmitters and cell signaling systems (pesticides, plastic derivatives, heavy metals, PCBs). The developing nervous system is particularly susceptible to disruption by toxins, and such disruptions may result in many of the symptoms of autism.

It is becoming apparent that through epigenetic mechanisms (such as the switching on or off of critical genes through effects of certain chemicals), parents may transmit to their children damage to genes acquired through environmental exposures. This may result in a syndrome that looks like a classical mutation, in that several children in a family may be affected. The critical difference is that these disturbed genes might be restored to appropriate functioning by vigorous detoxification and nutritional support of the parents before they conceive another child, thereby reducing the risk of having a subsequent special-needs child.

Healing in Autism

It can be (and often is) overwhelming to attempt to do everything possible to address a child's autism. The important thing is to decide what to do next, and then do it properly. For children with autism spectrum disorders, healing happens through removing obstacles and strengthening weak systems by supplementing for physiologic deficiencies and providing corrective therapies.

As Sid Baker, M.D., has said, "We seek to find out what the child needs to eliminate, and what they need to get more of. In doing so, we allow the body to return to a state of balance, restoring its incredibly intricate communication systems and repairing injured organs to the extent that is possible."

Autism: A Global Problem

Our society is finally looking deeper into the epidemic of autism. But it is just beginning to do so, as more professionals and influential people see their own children affected. This disorder is threatening to fiscally incapacitate our educational system and will place inconceivable burdens on the next generation if not solved. Even if the rate of increase of autism is halted now, the costs of caring for affected children growing into adulthood may be more than we can bear.

It is parents, hundreds of thousands of them in the United States alone, who will determine the fate of our children and, ultimately, of our society. Children need to have full access to all of the currently useful treatments. No longer can we tolerate the "head in the sand" approach of regulatory agencies to toxins, overuse of antibiotics and nutrient depletion of our soils and foods, all of which are contributing to this disease. We need to demand and receive vigorous funding from the government for relevant and unbiased research into the remaining unanswered questions about causation, prevention and treatment.

If we unite in purpose and make our voices heard, the undue burdens on our children that are causing this epidemic can be targeted and removed.

Note to Parents

Since committing my career to the treatment of children with autism, I have met more brilliant, amazing, dedicated parents than ever before, and have been deeply touched by the beauty and depth of these children and the boundless love of their parents. It takes a very special person to successfully parent a child with autism. I commend and bless all of you who have been given this assignment. May your child find healing in the years to come.

AUTHOR

John Green, M.D., is a specialist in clinical ecology and nutritional medicine and is a Defeat Autism Now! (DAN!) practitioner. He works in Oregon City, Ore.

Effective Treatments for Autism

BY DOREEN GRANPEESHEH PH.D., BCBA

While there is much controversy over the cause of autism, there have been remarkable advances in its treatment. In fact, study upon study shows that behavioral treatments rooted in applied behavioral analysis (ABA) yield significant positive results. In addition, the synergistic application of behavioral and medical treatments may allow children to acquire skills more rapidly, achieve more frequent positive outcomes, and actually lose their diagnosis of autism and be deemed recovered.

ABA now is the most recognized and scientifically supported treatment for autism. By changing the antecedents and consequences of behaviors symptomatic of autism, ABA specialists teach children the skills in which they are delayed, thereby replacing challenging and aberrant behaviors with functional and adaptive skills.

Research has shown that with early intensive ABA therapy, 47 percent of children with autism fully recover and lead healthy, happy lives. Many more show significant improvements in communication, skill acquisition and reduction of problematic behaviors. Sadly, delay in diagnosis and limited funding for this therapy have prevented most children from receiving this type of care. With the precipitous rise in the number of cases, there are long waiting lists for the most experienced therapists.

There is a strong body of evidence supporting a biomedical cause in the onset of autism. The dramatic rise in the incidence of autism in the last decade, without any concordant change in the diagnostic criteria, points toward environmental triggers playing a role in the genesis of the disorder. Many experts feel that exposure to toxins, along with the effect of certain medicines and an intense vaccination schedule on the immune system, can trigger a destructive cascade affecting crucial metabolic pathways. This cascade can result in significant immune and gastrointestinal symptoms and in turn can affect the way the brain functions.

Biomedical interventions that show promise may include ridding the body of poisons, lowering inflammatory states, reducing oxidative stress and normalizing the immune system. Functional interventions may include dietary therapies, nutrient support to help rebuild the body's gastrointestinal, immune and metabolic pathways, and detoxification of heavy metals.

These therapies can lead to a dramatic reduction in autistic and neurobehavioral symptoms. The outcome is children who are mainstreamed educationally and socially. While there still is a need for further research to verify the benefits of these biomedical treatments, many clinicians and parents have reported astounding results.

With early, intensive ABA and comprehensive biomedical treatments, children affected by autism can lead fulfilling, productive lives. Linking families and treatment experts through effective and early diagnosis, improved funding channels, community involvement and increased access to resources is key to facilitating these relationships and bringing hope to thousands of families.

Doreen Granpeesheh received her Ph.D. in psychology from UCLA and is licensed by the Medical Board of California and the Texas State Board of Psychologists. She is a psychologist and board certified behavior analyst, and has been providing behavioral therapy since 1979. In 1990, Granpeesheh founded The Center for Autism and Related Disorders (CARD) and through its 17 offices worldwide, has provided diagnosis, assessment and behavioral treatment for over 5,000 children with autism and related disorders.

ASA is calling for 2007 Board of Director Candidates to represent the Far West, Southwest and At Large positions. To nominate a candidate for consideration, please contact Ms. Ruth Elaine Hane, ASA Board Member, at chifields@qwest.net.

The Parents' Role *in Biomedical Treatment for Autism Spectrum Disorders*

BY LISA ACKERMAN

Nothing is more heartbreaking for parents than receiving the label of "autism" for their beloved child. Hopes and dreams for a child never include this devastating diagnosis. As follow-up appointments come and go, many families, including mine, have heard this statement from professionals: "There is nothing you can do."

Parents of newly diagnosed children are bewildered, because many children on the spectrum have medical symptoms that are not explained by an autism diagnosis. The child's doctors, who typically do not look beyond the autism label, rarely address these symptoms, including gut problems, allergies, rashes and others.

In the new millennium, in which doctors are capable of saving thousands of lives using state-of-the-art treatments, the evaluation and treatment of autism appears to be trapped in the Dark Ages. While much progress has been made in the past 20 years through the use of traditional therapies, including applied behavioral analysis (ABA), speech therapy, occupational therapy and other key therapies, little has been offered in the way of biomedical intervention and treatments for children on the autism spectrum. This is even more frustrating now that we are in the midst of an epidemic affecting one in 166 children.

There is good news, however. What I can share with parents of newly diagnosed children, and with families who have been on their autism journey for a while, is the knowledge that there *are* effective treatments—and there *is* hope.

Talk About Curing Autism (TACA) includes more than 2,100 families, many of which are exploring biomedical and alternative treatments. More than 40 TACA families have recovered children (meaning the child's diagnosis is no longer germane and they are indistinguishable from their peers), and more children are well on their way to recovery.

These successes are due to a combination of biomedical interventions and traditional therapies.

In many cases, families want to treat their children's medical issues, which can include lack of sleep or severe sleep disturbances; extreme gut disorders (often including alternating diarrhea and constipation); rare parasites, viruses, yeast overgrowth or bacteria; extreme allergies to foods or substances in the environment; unexplained rashes; sallow complexions; dark circles under the eyes; and behaviors that ebb and flow in patterns that may coincide with physical symptoms.

Most parents partner with knowledgeable and open-minded physicians to explore treatments that will address both the behavioral problems and the physical symptoms of their children. As key members of the treatment team, these parents play an important role in working with a variety of medical professionals.

The first and most crucial role parents have is selecting the medical team that will guide their child's treatment plan. In making this decision, it is important to understand that many doctors follow the guidelines of the American Academy of Pediatrics (www.tacanow.com/pdf/33%20-%20aap%20standards.pdf). These guidelines, which have not been updated since May 2001, discourage physicians from recommending the cutting-edge treatments that help many children with autism spectrum disorders because these approaches are considered "alternative."

This point is extremely important, because if a test or treatment is not recommended in the standards of care, the costs for testing and treating may be left up to the families. In addition, the professionals who work with our special children need to think "outside the box" to address children's biomedical symptoms and issues.

Selecting the right physician is just the first step that parents need to take in the journey toward a better life or even a full recovery for their child. The insight of parents is crucial in providing valuable clues about treatment priority, and providing this insight in a knowledgeable and organized manner can optimize treatment for the child with autism and save money, time and effort for families.

Following are the key steps parents can take as they participate in this medical treatment process:

I. Read. Parents need to read both books and information on Internet sites to prepare for their role in the treatment process. TACA offers the following online articles:

- "The Art of Managing Professionals & Appointments," and "Parent's Bill of Rights and Parent Responsibilities." This site includes interviewing questions and ways to plan for appointments: www.tacanow.com/managing_professionals.htm.
- "Why are DAN! (Defeat Autism Now!) Doctors So Expensive?" This site includes tips and tricks to prepare for medical appointments and testing: www.tacanow.com/dan_doctors_expensive.htm.
- A presentation on how to start biomedical intervention for autism spectrum disorders: www.tacanow.com/starting_biomed/default.htm.
- "What is it? When Something is Going On; Strange Behaviors, a Plateau, an Old Self Stims." This site provides a troubleshooting checklist for families in the biomedical process: www.tacanow.com/whatisit.htm.

Among the books that parents have found most helpful when beginning treatment are:

- *Unraveling the Mystery of Autism and Pervasive Developmental Disorder,* by Karyn Seroussi
- *Evidence of Harm,* by David Kirby
- *Is This Your Child? Discovering and Treating Unrecognized Allergies in Children and Adults,* by Dr. Doris J. Rapp
- *Children with Starving Brains, A Medical Treatment Guide for Autism Spectrum Disorder,* 2nd Edition, by Dr Jaquelyn McCandless
- *Autism: Effective Biomedical Treatments (Have We Done Everything We Can For This Child? Individuality In An Epidemic),* by Dr. Sidney Baker and Dr. Jon Pangborn
- *What Your Doctor May Not Tell You About Children's Vaccinations,* by Dr Stephanie Cave, with Deborah Mitchell
- Additional Web resources pertaining to biomedical treatments include:
  1. Autism Research Institute: www.autism.com/ari offers a list of Defeat Autism Now! (DAN!) doctors
  2. Thoughtful House – www.thoughtfulhouse.org
  3. International Child Development Resource Center (ICDRC) www.icdrc.org/www.gnd.org
  4. TACA www.tacanow.org (parent-to-parent information)

II. Get Educated. Attend a Defeat Autism Now! (DAN!) conference for the latest in medical research and information. For a listing of upcoming events, visit www.danconference.com.

III. Network. Talk to multiple families about the most recommended resources. Even though children with autism spectrum disorders have different needs and require individualized treatment protocols, input from other parents can be invaluable in providing reviews of resources, stories about successes or failures, and tips that could save time and money.

IV. Select a Partner You Like for the Long Haul. Interview several doctors before you choose one as your treatment partner. Since you will be working with this professional on a regular basis, it is good to pick someone you like and can communicate with effectively.

V. Document. Parents should document their child's history carefully so that they can give their doctor a complete record. It also is helpful to write a one- to two-page summary—a "Cliff's Notes" version of the child's file—that hits such high points as regression information, current medical therapies and traditional therapies, and key issues that need to be addressed. Copies of

recent behavioral or psychological assessments and the IEP (Individualized Education Plan) from the school district also will yield important clues for the doctor.

VI. Prioritize. Prioritize your child's issues when you address them with the physician. If your family is getting little sleep or your child has gut issues, these often are good places to start building a foundation for overall health. Then identify other issues that need attention. Your input is important in setting priorities so the doctor knows what should be the focus.

VII. Evaluate Costs. Take the guesswork out of this important question and find out. While costs may vary according to each child's unique medical issues, it is important to outline fees in advance for office visits (typically one to three per year), emergency/after-hours calls, phone consults, treatment protocols, lab fees and other items. Obtaining insurance pre-approvals for treatments also can be a lifesaver for the family wallet.

VIII. Emergencies. If a treatment causes side effects, parents should obtain clear guidelines as to whether they should call the doctor or emergency facilities. A description of non-serious side effects (continue the treatment) versus serious side effects (stop the treatment and/or call the doctor's office) should be clearly provided at the end of each appointment when starting a new treatment protocol.

IX. Read Some More. The education process will continue after your first year. It is especially important to read about each suggested treatment after a doctor recommends it and *before* you try it on your child. Research and information are rapidly changing in the medical treatment field and continuing your education is a necessity.

X. Evaluate Treatments. The treating professional should outline the positive and negative results a treatment could yield. Creating an easy-to-use "check-off" document outlining each day's treatment is extremely important in this process. This should include the following data: meals, bowel movements, liquids, medication, sleep patterns and behavior changes. Keep your daily journal in an easy-to-find place where you will see it and can easily jot down notes. Bring the journal on follow-up doctor appointments or have it handy during phone consults.

A Few Warnings. In the biomedical journey, a few words of caution are warranted:

1. Not These Words! Don't let the diagnosis of autism be an excuse for failing to treat issues that are medically necessary to treat. If a doctor says that a medical issue is "just part of the syndrome," it may be time to find a new resource.
2. How Long? Don't give up if you try only one or two treatments and they do not help your child. It's heartbreaking when I hear parents describe how the failure of a treatment led them to stop biomedical intervention altogether. Children on the autism spectrum are unique. The solutions to their medical problems are unique as well, and answers are still emerging. It is important to remember that the biomedical intervention process can take a long time to yield results, but these results can be amazing, if you use patience, a good doctor and medical test results to help design a treatment plan unique to your child's needs.
3. Charlatans. As in any growth industry there are sales people ready to sell you products, including medical treatments for your child. Work with your doctor and parent community to identify treatments for your child and verify good resources to use.
4. Trust Your Instincts. If something about a situation or office or medical professional does not feel right, it may not be. Do more research on the provider and ask other parents for feedback. It is important that parents never lose faith in their instincts in this process.

Some Final Words: Selecting Treatments. Medical treatments for children on the spectrum should be selected based on family history and patient intake (symptoms and history). Medical test results (current and past) also provide important markers.

Doctors should look at what the child has responded to, both positively and negatively. This information will yield important clues when it comes to selecting protocols unique to the child's needs.

Finally, based on the parent/child issues, doctors should:

- be able to set treatment priorities
- allow the parents to prioritize these treatments as a team

Biomedical treatment should be a key part of the intervention plan for a child with autism. In addition, consider one-on-one behavioral intervention, including applied behavioral analysis, verbal behavioral analysis, speech therapy, occupational therapy, and therapies to address play skills and social skills. Combining biomedical intervention and intensive one-on-one therapies can offer a comprehensive treatment approach for a child affected by autism.

AUTHOR

Lisa Ackerman is a parent whose experience includes one child: her son, Jeff. She has quit her job in management to work full time with her son and other families through a group she founded, Talk About Curing Autism (TACA). TACA started with 10 families in November 2000, and by August 2006 had more than 2,100 families and seven meeting locations in California. For more information about TACA, go to www.tacanow.org. Ackerman also does a bimonthly free online radio show at www.autismone.org/radio.

Autism's McGuffin

BY DAN OLMSTED

In Alfred Hitchcock movies, there's a characteristic plot device that the great director called a "McGuffin": What looks like the central premise of the movie ultimately has nothing to do with story.

The classic example is "Psycho," in which Janet Leigh steals $40,000 and goes on the lam, but ends up dead for reasons having nothing to do with the theft—and everything to do with the Bates Motel she had the misfortune to check into. It's an ingenious bit of misdirection.

After spending the last couple of years looking at the natural history of autism, I'm convinced that ever since the original case series was published in 1943, most mainstream research has fallen for the McGuffin.

Autism from the Beginning

Let's start at the beginning. One day in November 1935, a mother brought her 3-year-old son, Alfred, to Johns Hopkins University in Baltimore. "He has gradually shown a marked tendency toward developing one special interest, which will completely dominate his day's activities," she told the Hopkins medical staff, "and it is difficult to get his attention because of his symptoms."

After observing Alfred closely and seeing 10 similar children over the next few years, famed Hopkins child psychiatrist Leo Kanner wrote them up in his landmark 1943 paper, "Autistic Disturbances of Affective Contact." He said their common behavioral syndrome differed "markedly and uniquely" from "anything reported so far."

Kanner also noted commonalities among the parents. Alfred's mother, Kanner reported, was "very obsessive and excitable" and the father "does not get along well with people, is suspicious, easily hurt…" Overall, he remarked, "In the whole group there are very few really warmhearted fathers and mothers," and he later used the term "refrigerator parent," leading to an ugly stain of blame and guilt that, thankfully, has been discarded.

Another observation: "They all come from highly intelligent families," Kanner wrote. He acknowledged that "it is not easy to evaluate the fact that all of our patients have come of highly intelligent families." But it's safe to say that this idea— along with a handful of twin studies that are far less definitive than generally realized—paved the way for today's near-exclusive focus on genetics.

Considering the Environment

Blaming parents' genes certainly beats blaming parents' behavior, and that may in part explain the rush to embrace an exclusively genetic approach. But what matters most is truth. Kanner, blinded by the psychoanalytic bent of the day and his specialized medical background, simply and sadly overlooked a much more likely link: Several of Kanner's kids came from families where toxic exposure plausibly occurred. Let's take the cases in the order he presented them:

- Case 1: Donald T. was the son of "a brilliant lawyer." But as I've found in my own research, he was born in Forest, Miss., around the time the town was being replanted as a national forest.
- Case 2: Frederick W. was the son of a plant pathologist.
- Case 3: Richard M. was the son of a forestry professor at a southern university.

Once I found Donald's hometown, the idea that the first three cases shared some affinity to trees, nurseries and commercial agriculture seemed quite compelling. Still, I had no idea of a possible connection until Mark Blaxill of SafeMinds suggested a link via novel chemical compounds, in particular fungicides. He noted that Morris Kharasch, the research chemist who invented the ethyl-mercury-based vaccine preservative thimerosal in the 1920s, also patented ethyl-mercury-based fungicides at the same time. A ludicrous leap? Perhaps, but let's play out a "toxic connection" in those first cases:

- Case 4 was the son of a mining engineer. Heavy metals—mercury chief among them—are known neurotoxins.
- That brings us to Alfred L., arbitrarily listed as Case 8 in the series, although clearly the first to be seen at Johns Hopkins. His father? Yet another lawyer. But just as something else may have been going on with Donald T., the son of the "brilliant lawyer" from Forest in Case 1, there may be more to Alfred's story.
- Alfred's father, significantly, had dual degrees: he was a chemist as well a lawyer, according to Kanner. And he combined those skills in a perfect job: working for the United States Patent Office.

It is interesting that the first case of a novel disorder was the son of a chemist in the patent office. Who knows what compounds Alfred's father had his hands on, but is there any simpler definition of patent-worthiness than something "markedly and uniquely" different—Kanner's observation about the disorder itself?

Other Study Considerations

Perhaps autism was newly observed in the 1930s because whatever caused it was new too. Since I first wrote about the possibility of harmful exposures in Kanner's first 11 cases—a link that, as far as I know, had never been proposed—I've become aware of three studies that suggest a chemical connection in the subsequent rise of the age of autism.

In the 1976 book, *The Autistic Syndromes,* Dr. Mary Coleman described her study of 78 autistic children in which she noticed "an unusual exposure of parents to chemicals in the preconception period." Out of 78 autistic kids, 20 were from families with chemical exposure; four were from families where both parents had such exposures with seven out of the eight chemists. Still, Coleman worried that because the parents volunteered for the survey, they might have been scientifically inclined, skewing the results toward careers like chemistry.

To test that idea, one of Coleman's young associates, Thomas Felicetti, did his dissertation on a group of 60 children: 20 with autism, 20 with mental retardation and 20 "typicals," all enrolled at the Avalon School in Connecticut where he worked. The association held up: "The results did, in fact, suggest a chemical connection," Felicetti wrote in the journal *Milieu Therapy* in 1981.

"Eight of the 37 known parents of the autistic children had sustained occupational exposure to chemicals prior to conception. Five were chemists and three worked in related fields. The exposed parents represented 21 percent of the autistic group. This compared to 2.7 percent of the retardation controls and 10 percent of the normal controls. …The data, subjected to statistical analysis, demonstrated a chemical connection."

In the 2002 book, *Impact of Hazardous Chemicals on Public Health, Policy, and Service,* the authors review those studies and cite another—an unpublished manuscript by Marcus and Broman: "They found a higher incidence of occupations involving exposure to chemicals among the parents of children with autism."

Let's review our story so far: The first autistic child to come to Leo Kanner's attention in 1935 was the son of a chemist-lawyer at the patent office. Signs of novel toxic exposures suggest themselves in other children in that first cohort. By the early 1980s, subsequent studies found, again and again, a striking proportion of parents with clear chemical exposures.

Genes certainly could play a susceptibility role in this scenario, "loading the gun," as the geneticists say. My point simply is that the fingerprints of harmful exposure are all over the trigger in many early cases.

So here's my question: Why has this alarmingly plausible hypothesis—evident as early as Alfred L.'s chemist father in 1935—all but disappeared from the research radar, while increasingly arcane gene studies get the attention and money?

Guess what. The parents didn't do it. It's time to spot the McGuffin in this mystery.

AUTHOR

Dan Olmsted is an investigative reporter and senior editor for United Press International (UPI).

Exploring the Role of Toxicology in the Etiology of Autism:

A View from the Spectrum and a Call to Action

BY STEPHEN SHORE

After developing typically for the first 18 months of my life, I lost functional communication, began having tantrums, exhibited self-stimulatory behaviors, withdrew from the environment and developed a great fear of change. In short, I experienced regressive autism. At the time of my diagnosis in 1964, the incidence of autism was considered to be no more than four in 10,000; further, the disorder was believed to be caused by poor mothering.

Throughout my public school years, as far as I knew, I was the only child who had autism. Knowing what I know today, I'm sure some of my classmates would have been considered to be on the autism spectrum, but even with that, we were but a mere handful of students

Today we have an explosion in the number of children on the autism spectrum, to the point where the U.S. Centers for Disease Control and Prevention recognizes an incidence rate of 67 in 10,000, or 1 in 166 children. These rates are reflected in our schools, where we now have entire classrooms devoted to children with pervasive developmental disorders. In fact, within bicycling distance of my home in Boston, there are two private schools, each with enrollments nearing 150 students that are exclusive to children with autism.

Autism originally was thought to have a maternal psychological etiology, but thanks to the hard work of Dr. Bernard Rimland and those following him, it now is known that the only thing mothers may have to do with causing their child's autism is possibly passing on some genetic material. Current research seems to point to the etiology of autism beginning with a genetic predisposition, which then is triggered by other factors. This theory of genetic predisposition explains why autistic tendencies commonly run in families, just as they do in mine.

Genetics is a good place to start to determine predisposition to autism and other related neurobiological conditions. However, genetics doesn't change so fast in a single generation as to explain such a dramatic increase in autism. There must be another explanation.

I often wonder about the role of environmental toxins in causing my autism. Some autistic traits and other genetic preconditions exist in my family, but with the exception of my brother, two years my senior and diagnosed with mild to moderate retardation, no one can be considered as having autism.

Might it have been a vaccine? It could not have been the MMR (measles, mumps and rubella) because that combination of vaccines didn't exist when I was a child. However, there was DTP, with its complement of thimerosal—a mercury-based preservative that more recently had been added to some childhood vaccines, including MMR. (Thimerosal has since been removed from most vaccines due to concerns about its potential impact on children.) Might it be that my autism was triggered by another environmental toxin?

Some researchers consider greater awareness and a broadening definition of "autism" to explain the rise in the incidence of the disorder. Yet another explanation may be "political distortion," wherein a child having some autistic tendencies is given a spectrum diagnosis because professionals and parents realize that this may be the only way the student receives the full complement of educational services he needs. While these reasons may explain an elevation of a few percentage points, the cause for the rest of the increase remains unanswered.

Although I am unable to prove that the autism triggered within me was due to environmental toxins, two important facts are clear: 1) We have a much higher incidence of autism now than when I was in grade school, which cannot be explained through better diagnosis or genetics, and 2) even though the research is not conclusive on whether mercury and other toxins are a cause of autism, it seems to make sense to remove these substances from the environment for the well-being of the entire population.

The need to examine the role of environmental toxins goes far beyond autism and other neurobiological conditions. By clarifying the effects of toxins and eliminating them, we all will benefit from having a cleaner environment so that we can lead more fulfilling and productive lives.

AUTHOR

Stephen Shore, an adult on the autism spectrum, is completing his doctoral degree in special education at Boston University. Stephen presents and consults internationally on issues about adults with autism. An ASA board member and president emeritus of the Asperger's Association of New England, Stephen serves on the board of director for Unlocking Autism, the Autism Services Association of Massachusetts, MAAP and the College Internship Program.

Rescuing a Generation

BY J.B. HANDLEY

My wife Lisa and I started Generation Rescue (www.generationrescue.org) in May 2005 out of gratitude. We felt intense gratitude for the parents of children with autism who came before us, particularly in the early days of the epidemic, and moved forward, blindly and against great adversity, convinced that their children's autism was not a genetic life sentence.

They knew, before the Defeat Autism Now! (DAN!) protocol even existed, that their children were very sick, physically sick, and that the physical sickness and the behaviors labeled autism somehow were related. It's because of them, and pioneers like Dr. Bernard Rimland, that Generation Rescue exists today.

We felt so lucky that our son, Jamison, was diagnosed in 2002 rather than 1992. Of course, parents of children with autism know that "lucky" is a relative term. From the first day that we realized something was wrong with our son, we had two amazing tools at our disposal: information and informed parents. The Internet helped make all this possible, and it allowed us to save precious time that we instead could use to begin healing Jamison.

Because of all this useful information, Jamison was able to see a DAN! doctor before his official diagnosis. Every decision we made on treatment was weighed with the input of dozens of highly informed parents giving us their advice in discussion groups. We were amazed and grateful for how many other parents were selflessly willing to help our son.

This gratitude led to a simple idea: Let's put all this information, and these great parents, in one place. And that's Generation Rescue. It's an organization that seeks to provide every helpful document we ever read on science and treatment for autism. And it brings together more than 350 families, in more than 20 countries, who are available to help other families get started after an autism diagnosis. These "rescue angels" are the soul of our organization, and they have helped more than 10,000 families begin the road to recovery for their children.

Autism is a reversible disorder. Our children improve, and many recover to go on and lead normal lives. Parents spend a lot of time fighting, both amongst themselves and with the outside world, about the cause of autism. Our Web site, however, is clear on what my wife and I believe caused our son's autism: vaccines and the mercury in them. Not every parent agrees with us.

For a parent of a child with autism, cause is a secondary concern. The big question facing all of us is simple: What can I do right now to make my child better? I believe that addressing the underlying physical conditions contributing to the diagnosis of autism will have the greatest impact on the trajectory of your child's recovery. For us, righting Jamison's diet, healing his gut, ensuring proper nutrient support, and detoxifying heavy metals and viruses from his body have had the greatest impact on the arc of his recovery.

> "These 'rescue angels' are the soul of our organization, and they have helped more than 10,000 families begin the road to recovery for their children."

If you have not considered biomedical treatment, I hope you'll take a look at Generation Rescue's Web site and consider contacting one of our rescue angels or scheduling a visit with a DAN! doctor. Perhaps one day soon, you too will be expressing your gratitude for the growing network of parents and doctors who helped you treat your child.

AUTHOR

J.B. Handley and his wife Lisa founded Generation Rescue in May 2005. Learn more about the organization at www.generationrescue.org and www.putchildrenfirst.org.

There is Hope

BY JUDY CHINITZ GORMAN

"Autism is a lifelong disability." "Autism is not curable." "You must learn to love your child as she is." Parents typically hear words like these from doctors when their child is diagnosed with autism. In essence, they are asked to give up the hope of recovery for their child.

Yet mounting evidence shows that most children diagnosed with autistic spectrum disorders can be helped, and some can even be cured. Many families are discovering that with the proper biomedical and educational interventions, coupled with hard work and devotion, children once written off as "untreatable" can lead happier, healthier and more independent lives.

Here are the stories of three such families—the Youngs, the Duffields and the Lewises—whose dedication and refusal to lose hope will result in better futures for their children.

The Young Family

Nikolai Young was born in June 1998. At 12 hours of age, he received a hepatitis B vaccine and immediately began to change. He stopped sleeping normally and screamed when he nursed. At three months, he had massive, bloody diarrhea. A sigmoidoscopy (an internal examination of the lower large bowel, or colon), showed severe colitis.

Over the next few years, Nikolai was constantly plagued with constipation, occasional diarrhea, eczema, rectal abscesses, stomach bloating, distention and unexplained episodes of high fevers. He never slept through the night, displayed severe emotional fluctuations (sometimes laughing for no reason for hours at a time), had no eye contact and was extremely hyperactive. He was diagnosed with autism at 33 months of age. The diagnosing pediatrician told Nikolai's parents that his disability was life long, and that he would require care throughout his life.

George, Nikolai's dad, is a physician. While his mother, Robin, immediately dove into research, believing fully that the many vaccines Nikolai had received were responsible for his condition, George initially did not agree. It just didn't seem possible to him. But he started to read, he started to ask questions, he went to a Defeat Autism Now! Conference, and he too came to believe that Robin's instinct was correct.

The Youngs quickly began biomedical interventions. Nikolai was put on a casein- and gluten-free diet. Almost immediately, his language began to improve. All foods to which he had tested sensitive were removed from his diet. Over time his parents added supplements, vitamins and antifungals to his daily regime, and enrolled Nikolai in an intensive educational program.

Nikolai's improvements were amazingly rapid. Within 10 months of starting biomedical treatment, he had lost his autism diagnosis. He still had residual language and social delays, but he continued his remarkable recovery.

He is now eight years old. His mother writes: "Nikolai is now entering the second grade. We just returned from a week at Rock Springs Guest Ranch, a dude ranch in central Oregon. Nikolai and many other children were in their kids' program, where college students and older counselors have the kids in many group activities from morning until night. Nikolai won the 'glass half full' award—given because he is always so upbeat and happy and looks at things in such a positive light. The youth program director said, 'We just love him.'"

She adds, "At our year-end conference at his school, the teachers told us many, many positive things, but the bottom line is that they would welcome him back to the school with open arms. However, we are transferring him from a private school to our new, local public school. We made this decision because the private school currently goes only through sixth grade, and although it is an excellent school, we were concerned about the transition in the tough pre-teen/teen years and want him to have lifelong friendships in a community, rather than be in a 'commuter school' situation."

Robin reports that Nikolai's abstract conceptualization skills are "quite sophisticated," and that his social skills with peers are "fine." She concludes, "We go forward from here, thankful that we have our wonderful son Nikolai fully present in our lives and our world."

The Duffield Family

Michael Duffield was a healthy and happy one-year-old in 1999, when his parents, Julie and Joe, found out they was expecting their second child. Michael was the perfect baby, in fact, except for his frequent ear infections and the subsequent rounds of antibiotics he received to combat them.

At 18 months, Michael was brought in for his well-baby visit and given four vaccines. Within four hours, he was running a fever of 104. He continued to run high fevers for three months—the record being 105.7 degrees—and during this time he lost all of his social skills. He developed severe auditory sensitivities. He no longer seemed to understand when spoken to, and his own speech devolved into grunts. Michael rapidly deteriorated physically as well. He lost weight, stopped sleeping and, worst of all, began to engage in severe self-stimulatory behaviors.

Two weeks before the Duffields' second baby was born, Michael was diagnosed with autism. "Therapy is the only option," they were told. "Autism can't be treated; it is life long."

The Duffields were not willing to give up on their little boy. Quickly they learned that various biomedical interventions were said to benefit children like their son, and they set out to try them.

Three days on a casein- and gluten-free diet restored some eye contact and allowed Michael to sleep through the night again. The Duffields joined the Mother's Milk Club of Utah, and with donations of breast milk from that organization, combined with what Julie could spare, they began to feed Michael breast milk to restore his damaged immune system. The ear infections stopped, and his autism began to fade. Other treatments—minerals, vitamins, chelation and secretin—also had profound effects on Michael's symptoms.

While struggling with Michael's behavioral and physical symptoms, the Duffields noticed that their little daughter, Jessica, did not seem to be developing on schedule. By 13 months of age, she too began to severely regress. She completely stopped babbling. She no longer imitated songs, knew her own name or made eye contact. Even her muscle tone completely regressed.

At birth, Jessica had been given a hepatitis B shot, which caused her to develop lesions in her mouth and rectum. One doctor suggested that the lesions actually might run through the entire digestive tract. After that reaction, the Duffields opted to not give Jessica any more vaccines—but they believe one was enough to harm her. She was diagnosed with autism at 17 months of age. Immediately, she was started on chelation therapy and other medical treatments.

Now, six years after Michael's diagnosis, and four years after Jessica's, Julie offers this update on her two children: "Jessica is a fabulous writer and speller, and she's going into 1st grade next year. She no longer qualifies for the autism unit, but she's in a classroom with more staff that puts emphasis on reading. She loves to read, and I think she'll thrive. She has a best friend down the street, and they have sleepovers and play regularly."

For Michael, progress is coming more slowly, but he continues to improve. "Michael is still struggling to understand what we say and repeat it back," Julie says. "His hearing is so hypersensitive, he gets the sounds jumbled. But he has the theme songs to the movie "Cars" memorized (slightly altered pronunciation, but he does the drum and guitar sounds too). He loves to play games and swim. He's gotten over many of his fears of waterslides and getting his head in the water."

Julie, who has documented her family's story at www.autismmedia.org/new/media10.html, adds, "I can't believe how wonderful our lives are. I hoped for my kids, but to see them so happy and playful just makes my heart soar. I hope with all my heart that parents will be able to find out what is going on in their children, since each case is so different, so that all these children might enjoy healthier and more productive lives."

The Lewis Family

Brian Lewis was a difficult infant. He didn't cry like a normal baby. Feeding was very hard; the slightest distraction—a fan moving, someone walking by—would cause him to stop eating and to scream. His developmental delays were apparent by the time he was 15 months old. He could not crawl or walk, and even had difficulty sitting up. He didn't babble. Despite every intervention his parents, Carolyn and Allen, could think of, he would tantrum for hours at a time. Nothing would comfort him.

When Brian was 22 months old, a pediatric neurologist diagnosed him as having a pervasive developmental disorder. Just before his second birthday, that diagnosis was changed to full autism.

Carolyn began doing extensive research into treatment possibilities for their sick son. It took Allen a long time to come to believe there was the chance of a cure. A pediatrician by trade, he was not taught to believe in the idea that autism could be treated. As is the case in so many families with children who are autistic, their initial disagreement at first led to tensions between them.

However, a casein- and gluten-free diet led to an immediate improvement in eye contact for Brian. He quickly began to show other signs of improved health; for example, his nose stopped running. Even more dramatically, his once-perpetual tantrums ceased over the next few weeks. Carolyn realized that Brian also was reacting to various other foods, including corn, soy, eggs, citrus fruits and tomatoes, and they were eliminated.

Like Nikolai, Michael and Jessica, Brian never slept through the night. In fact, he spent much of the night screaming. He too suffered from multiple ear infections, which eventually lead to the insertion of tubes. At 22 months, he had a second set inserted along with a tonsillectomy and adenoidectomy. Two days after the surgery, Brian slept through the night for the first time.

Dietary interventions, nutritional supplements and education have made all the difference with Brian, according to his family. Carolyn says, "He is doing very well in mainstream first grade, which he attended without the need for an aide. He behaves as a typical six-year-old most of the time. He is very popular with his classmates and was continually invited for play dates."

She adds, "While he still has some deficits, he is catching up quickly. He is very social, has a great imagination, plays well with others and has a great sense of humor." His interests, she says, have expanded to include much more than his previous obsession with trains. These days, he's interested in sports, science, construction, animals, games and art.

"We continue dietary and biomedical interventions, which have proven to be extremely important for Brian. It took years to find the right supplements in the right amounts for Brian to be his best. The most important supplements have been cod liver oil, probiotics, zinc, B6 and MT Promoter (compounded at Pfeiffer Treatment Center)," Carolyn says.

Brian's diet continues to be free of gluten, soy and citrus fruits, because he reacts to those foods. The family also chooses to avoid hydrogenated oils, dyes, MSG, nitrates, food additives, preservatives and pesticides. They prepare most meals and snacks at home from the healthiest ingredients available.

Brian, the child who once was so difficult to feed, now eats a varied diet including plenty of fruits and vegetables. "He eats many healthy foods in a variety of colors and textures with only an occasional protest. We are able to eat out at restaurants every week as a family, and it is a relief that there is always something for Brian to select from the menu!" says Carolyn.

Many interventions have contributed to Brian's success, Carolyn adds. "His big sister Rachael is also a huge help, as she has taught him so many things with great understanding, patience and unconditional love." Carolyn also credits a network of supporters: "Thanks to the help and insight we have received from friends and colleagues all over the country, our family is now enjoying a much more normal life!"

These families and more than 30 others tell their stories in *Recovering Autistic Children,* edited by Stephen M. Edelson, Ph.D., and Bernard Rimland, Ph.D., and published by the Autism Research Institute (second printing, 2006).

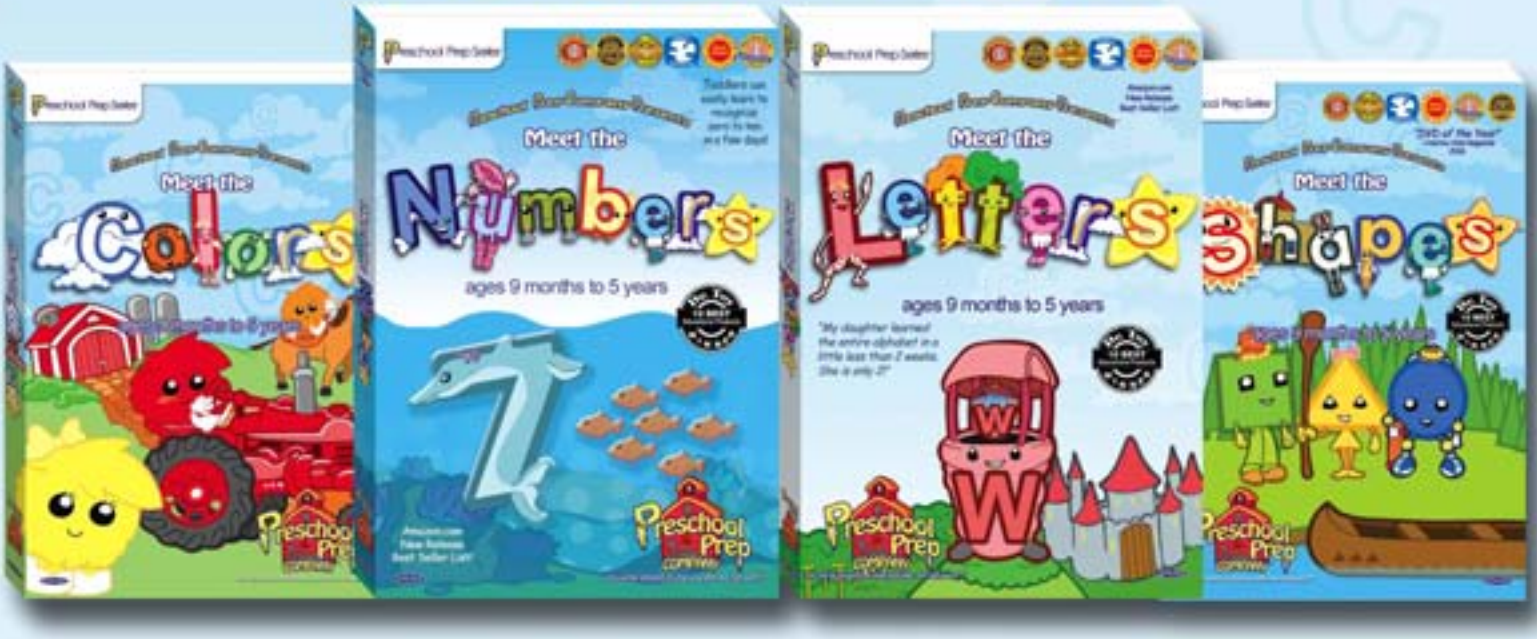
AUTHOR

Judy Chinitz Gorman is the parent of two sons, one of whom has autism. She holds a master's in special education and is currently pursuing another in nutrition.

AWARD WINNING

Preschool Prep Series Products

Dr. Toy 10 BEST Educational Products WINNER



"My four year old son LOVES your DVDs. He is autistic and didn't know any letters before he watched. He now knows all of his upper and lowercase letters because of *Meet the Letters!*"
- Ashley Robertson

"Before, watching *Meet the Numbers* he could only count to 3. He now counts to 10 easily! His speech therapist told me that because of this he is more focused in his sessions."
- Martha Blake

A study of over 50 babies and toddlers, who watched *Meet the Letters*, resulted in over 90% of these children having complete upper and lowercase letter recognition. Many learned in less than two weeks! Most impressively, nearly 70% of children under 24 months of age mastered the alphabet.

"Our youngest son was diagnosed with mild autism and has a speech delay. Before watching *Meet the Letters* he could only say 10 to 20 words. After watching *Meet the Letters* he started humming and singing the alphabet. His therapist noticed a change immediately."
- The Lazaro Family

"My 3 year old son is autistic and has learned all of his upper and lowercase letters from watching *Meet the Letters*. He points at the TV and says letter names the whole time he is watching. I was amazed at how he responded to this wonderful learning tool."
- Karen Richards

Preschool Prep COMPANY

ADVOCACY

LEGISLATIVE WRAP UP ON AUTISM ISSUES

Congress recessed in September so that members of Congress could return home to campaign for re-election. While Congress was able to complete some of its legislative business in September, much work still remained to be done in a lame-duck session. As this edition of the *Autism Advocate* went to press, the following were on ASA's legislative radar as issues of interest to the autism community.

DEFENSE APPROPRIATIONS

Prior to recessing, Congress passed the FY 2007 Department of Defense Appropriations bill. This legislation includes funding for a range of biomedical research projects, and for the first time, dedicates $7.5 million to autism-related research. This program is funded under the Army's Research, Development, Education and Training Center, which supports innovative, cutting-edge research for a range of conditions including cancer, spinal cord injury, diabetes, Parkinson's disease and other diseases and disabilities.

While funding will support research on autism spectrum disorders in the military, breakthroughs in this area—such as improved diagnosis, early intervention, and treatment—will have broad application for the larger autism community.

COMBATING AUTISM ACT

The Senate unanimously passed S. 843, the Combating Autism Act (CAA), in early August. This important legislation would provide an additional $900 million for autism related research at the NIH. It would bolster efforts to improve diagnosis, early intervention, and treatments for autism spectrum disorders.

Despite the widespread support of the autism community, unanimous support in the U.S. Senate, and broad, bipartisan support in the House, the legislation remained tied up in the House Energy & Commerce Committee. Congressman Joe Barton (R-Tex.), chairman of the powerful Energy and Commerce Committee, refused to pass the Combating Autism Act because he had different political priorities.

ASA did not given up the fight on the Combating Autism Act, and worked to convince Chairman Barton, Speaker Hastert, and the House leadership to move this legislation. ASA advocates sent tens of thousands of emails, letters and phone messages to their members of Congress, urging them to convince Chairman Barton and the House leadership to pass CAA. ASA's staff and volunteer leadership lobbied many members of Congress and worked with our Congressional champions, the Coalition for Autism Research and Education (CARE), to get this bill through the House of Representatives and onto the President's desk.

As of press time, ASA continued to keep up the fight on this important issue.

LIFESPAN RESPITE CARE ACT

Similar to the Combating Autism Act, the House of Representatives failed to enact H.R. 3248, the Lifespan Respite Care Act. This legislation would establish a program to assist family caregivers in accessing affordable and high-quality respite care. Respite care provides parents, grandparents, siblings and other caregivers the relief they need to cope with providing full-time care for individuals with disabilities. With respite care, family members are better able to maintain their own health, prevent family problems, keep their marriages intact and avoid costly institutional and long-term care.

This legislation was passed unanimously out of the Energy & Commerce Committee, but has not passed the House of Representatives. Unlike the Combating Autism Act, however, the House leadership has pledged to pass this legislation in the lame duck session (the so-called "lame duck" session covers the period of time after the November elections until Congress is convened in January). ASA has joined with a coalition of other disability related organizations to push for enactment of this important legislation.

FAMILY CAREGIVER SUPPORT ACT

After months of negotiations and compromise involving the House, Senate and the Bush Administration, the Older Americans Act has been reauthorized for five years, including the Family Caregiver Support Act. The act is an improvement over the 2000 reauthorization which authorized caregiver support, such as respite care, for older individuals caring for a child with a disability. Following the 2000 reauthorization, the Administration had defined children with disabilities as only those up to age 18, despite Congressional intent that older caregivers caring for adult children with disabilities receive the supports. The new law defines children with disabilities to include those over age 18 and reduces the caregiver age to 55. This will be a tremendous support to older caregivers still caring for their adult children with autism at home.

ADVOCACY

POST-KATRINA EMERGENCY MANAGEMENT REFORM

Before leaving for their districts, the Congress passed the FY 2007 Department of Homeland Security appropriations bill (HR 5441), which includes the Post-Katrina Emergency Management Reform bill. The disability community, including ASA, supported the establishment of a Disability Coordinator to ensure that the needs of individuals with disabilities are being properly addressed in emergency preparedness and disaster relief. Responsibilities of the Coordinator include: providing guidance and coordination on matters related to individuals with disabilities in emergency planning requirements and relief efforts; consulting with organizations that represent the interests and rights of individuals with disabilities about the needs of individuals with disabilities; ensuring the coordination and dissemination of best practices and model evacuation plans for individuals with disabilities; ensuring the development of training materials and a curriculum for training of emergency response providers, and providing guidance and implementing policies to ensure that the rights and wishes of individuals with disabilities regarding post-evacuation residency and relocation are respected. The Act also amends the Robert T. Stafford Disaster Relief and Emergency Assistance Act by inserting "disability" into its nondiscrimination clause.

OTHER AUTISM FUNDING ISSUES

Another issue on the agenda for the lame duck session is completion of the FY 2007 Labor, Health and Human Services and Education Appropriations legislation. Both the House and the Senate have reported their versions of this important spending bill out of committee. However, due to funding shortfalls, neither the House or the Senate has passed their versions on the floor. It is possible that this bill will be included in an end-of-year omnibus appropriations bill, or that it may be pushed off until next year.

Currently, both the House and the Senate bill provide funding for the CDC's autism program, which funds autism surveillance (counting the number of individuals with autism), early diagnosis and treatment programs and professional education programs. Despite the growing need for these types of activities, the House provided only $15.5 million for this critical program, the same as the funding level for FY 2006. The Senate also provides continuation funding, but does not provide funding to expand this important program.

Autism research at the National Institutes of Health was similarly shortchanged. Funding for the entire agency was cut by approximately $300,000, but funding at the leading autism institutes—the National Institute of Child Health and Human Development and the National Institute of Deafness and Other Communication Disorders—was cut by almost $10 million. While the Senate bill provided some additional funding for these activities, autism research continues to be underfunded.

With control of the House and Senate hanging in the balance, it is unclear whether Congress will enact appropriations bills in the lame duck Congress or will defer these hard decisions until January. ASA will certainly continue its efforts to secure additional funding for these critical autism related programs, and will alert our advocates about any progress on these important bills.

ASA BOARD APPROVES LEGISLATIVE AGENDA

Agenda to Guide Organization's Government Relations Activities

At its September board meeting in Phoenix, ASA's Board of Directors approved a comprehensive legislative agenda to guide the organization's government relations activities for the coming year. The document covers five core areas:

- Increasing awareness of autism issues
- Ensuring funding for autism activities
- Strengthening autism research
- Improving educational opportunities
- Providing critical services across the age span with renewed emphasis on issues related to adults with ASD

"This legislative agenda clearly articulates our desire that Congress and the Bush Administration tackle the issues affecting individuals with autism and their families by increasing appropriations, passing the Combating Autism Act and ensuring services across the lifespan," stated ASA Board Chair Cathy Pratt, Ph.D. "In particular, ASA is concerned that, along with research activities, service

systems are not adequately funded or prepared to support individuals with autism."

ASA President and CEO Lee Grossman, concurred, adding that ASA will be working with the congressional Coalition for Autism Research and Education (CARE) to ensure that individuals with autism are considered in discussions of reform to Social Security, Medicaid and other federal programs. "Health insurance coverage, education, employment, housing and community supports are all fundamental to an individual or family's quality of life," he said. "ASA will continue to push for research and services that result in effective practices and high-quality supports."

ASA'S NEW ADVOCACY WEB PAGE NOW LIVE

Get Up to Date on ASA's Government Relations Activities

ASA has been the leading organization representing the autism community in the nation's capital for more than 30 years. The efforts of ASA's leaders and staff over this time have resulted in the successful launch of a number of pieces of legislation affecting the autism community. Our work not only increases public awareness about autism, but has also resulted in millions of dollars devoted to autism research and services.

Now, we have updated our advocacy page, which is live on our Web site. Get informed on the latest developments on Capitol Hill by clicking "Get Involved" on the tool bar above, then clicking "Advocacy." Here, you will see a brief introduction about ASA's advocacy efforts, along with links to the five core areas of our legislative agenda, recently approved by the ASA Board of Directors.

ASA is continuously monitoring the activities of Congress and the federal government, educating these groups about the unique needs of those with autism and pushing for increased attention and programs. We are dedicated to this now and into the future. As always, we will keep you informed about of our activities through ASA's Web site; our magazine, The *Autism Advocate;* and through our "Action Alerts," which are often included as action items in our bi-weekly, free electronic newsletter, *ASA-Net.*

To view the advocacy page, go to: www.autism-society.org/advocacy

ASA 2006 NATIONAL CONFERENCE WINS *TRADESHOW WEEK'S* "FASTEST 50"

Exhibits at Conference Touted Highest Number Yet

Tradeshow Week announced that ASA is one of the "Fastest 50 Winners" in its 4th annual competition. ASA received this honor due to its impressive trade show and exhibition in Providence, Rhode Island, as part of its 2006 National Conference in July. Over 135 exhibiting companies and over 150 exhibitors presented at this conference, including publishers, centers for autism research, toy manufacturers, and the like. In addition to a variety of booths, ASA's exhibit hall also included plays and demonstrations throughout the 3-day event.

"We are grateful for this honor by *Tradeshow Week* and extremely appreciative of our conference exhibitors and ASA members who made this conference a success," said ASA President and CEO Lee Grossman.

The annual TSW Fastest 50 honors those shows that experienced the greatest growth in terms of net square footage over the preceding three years. All 50 winners will be honored during a weekend celebration in Boston. For more information, please visit http://www.tradeshowweek.com/.

ASA REGIONAL MEETINGS AND CHAPTER LEADER DEVELOPMENT WORKSHOPS WELL RECEIVED

ASA Members Receive Specialized Training on Autism Issues

ASA chapter leaders, special educators and parents from the Mid-Atlantic came together in early October in Virginia Beach to learn about positive behavioral supports for children with autism. The workshop, lead by ASA Board Member and Panel of Professional Advisor Co-chair Jim Ball, gave important strategies for communicating with children across the spectrum and optimizing their education programs in the classroom, as well as classroom tips for immediate use. ASA staff members Jeff Sell, Edward Shipley and Marguerite Colston also led a regional chapter leader development workshop that gave chapter leaders tools and information on advocacy, message development, handling the media and governance.

In late October, ASA and the Autism Society of Middle Tennessee hosted Paula Kluth, Ph.D., and over 110 special educators and parents for a day long training in Nashville. Dr. Kluth teaches not just inclusion, but including, and each person left at the end of the day with new ideas and a rejuvenated spirit on how to include those with special needs, especially autism, in their classrooms.

In related activities, many who attended the 2005 national conference in Nashville have inquired about "that singer from the opening session." That singer is Tammy Vice and when she is not assisting at ASMT events, working in the ASMT office or raising her family, she is a recording artist. Available now, "Breaking the Chains," is an acoustic collection of

—continued on page 69

CONFERENCE/NEWS

songs with many "I've been there" moments for the whole family. Vice says that the project is dedicated to individuals on the autism spectrum and those who love them. The song "Fittin' In" was written by Julie Herndon, a young adult with autism. For additional information, go to www.tammyvice.com. A portion of the proceeds goes to ASMT.

AUTISM SOCIETY OF AMERICA AND AUTISM RESEARCH INSTITUTE ANNOUNCE PARTNERSHIP TO ADDRESS EPIDEMIC

Two Organizations Founded by Dr. Bernard Rimland Join Together to Promote Cutting-edge Research and Service Delivery in the Autism Community

ASA and the Autism Research Institute (ARI) recently announced a strategic partnership to collaborate on conferences, publications and services that will improve the lives of all those affected by autism in the United States. By joining forces, ASA and ARI aim to continue the important stewardship of their founder, Dr. Bernard Rimland. A pioneer in the area of autism diagnosis and treatment, Dr. Rimland transformed the prevailing pessimistic view of autism in the medical and scientific community and built the largest parent support organization in the United States.

"Bernie Rimland was among the first to realize the importance of combining a focus on medical interventions with treatments, supports and services," stated Dr. Cathy Pratt, ASA Board Chairperson. "There is not one parent or professional who has not been impacted by the knowledge, dreams and thinking of Bernie Rimland. The ASA/ARI partnership is our way of ensuring that Bernie's vision will continue to guide the autism community for the long-term."

A major purpose of the ASA/ARI partnership is to promote awareness that autism must be treated as a whole body condition. Projects in 2007 will include biomarker conferences, distribution of scientific journals and collaborative efforts to serve over 100,000 members and supporters of these two organizations.

"I founded ASA in 1965 as a parent advocacy organization to work on behalf of autistic children and their families at local, state, and national levels," said Dr. Rimland. "I founded the Autism Research Institute in 1967 to conduct and sponsor scientific research on the cause and treatment of autism. ARI, through its Defeat Autism Now! (DAN!) project, has made enormous progress in the past few years—hundreds of the DAN! doctors and thousands of parents world-wide have reported bringing dramatic improvement, and sometimes recovery, of formerly autistic children. It is clearly time for ASA and ARI to capitalize on the progress that has been made. My colleague, Dr. Steve Edelson, with whom I have worked for 25 years, will play a major role in these efforts."

Lee Grossman, President and CEO of ASA, and Edelson, Associate Director of ARI, will oversee this strategic partnership.

This special issue of the ASA *Autism Advocate* was made possible by a grant from the John Merck Fund, a charitable organization which fosters research and advocacy in fields including developmental disabilities and environmental health.

The John Merck Fund was established in 1970 by the late Serena Merck, the widow of George W. Merck, former president of Merck & Co., as a family foundation. Since its inception, the fund has been committed to funding scientific investigation into the causes of developmental disabilities, as well as to providing support for families caring for developmentally disabled individuals. Among its endeavors, the fund provides four-year grants to outstanding young researchers in the areas of neurobiology and cognitive science, and annually presents the Serena Merck Award to an individual who is a role model in the day-to-day care of children who are both mentally and emotionally challenged.

In 1987, the fund expanded into several new areas, including an environmental program which has evolved to focus in large part on health issues. "Science is increasingly linking exposure to chemicals in the environment, including consumer products, to disease and disability," says Ruth Hennig, executive director of the fund. "If we can reduce or eliminate these exposures, we can also reduce or even prevent serious health problems including developmental disabilities." The fund is continuing its efforts in research and treatment, she says, but is also greatly expanding its efforts to address "upstream" causes of disabilities such as toxic chemicals in the environment.

One of the fund's goals, she says, is to enlist the aid of medical professionals, as well as patients and their families, in bringing attention to the issue of environmentally-caused illnesses. To that end, the fund has been making grants to major organizations in the learning and developmental disabilities communities for the past three years.

"We were delighted when the Autism Society of America approached us and expressed an interest in this effort," she says, noting that the contributions of ASA and other health organizations will help to put a new face on the issue of toxic exposure by showing that chemical pollution is not just an environmental problem but a health problem of major significance as well.

ASA thanks the John Merck Fund for its support of this project, and thanks the Merck family for their long-term dedication to helping individuals with developmental disabilities, their families, and the medical professionals working on their behalf.

Fighting for Our Children: Advocacy in the Age of Environmental Awareness

BY BERNARD RIMLAND, PH.D. (DR. RIMLAND WROTE THIS ARTICLE BEFORE HIS PASSING IN NOVEMBER 2006)

When I first began studying autism, after the 1956 birth of my son Mark, who has autism, every textbook and every doctor said the same thing: "Recovery doesn't happen." They were wrong about just about everything else, but they were right about that one fact —at the time, autism was a "hopeless" diagnosis.

Today, many parents of children with autism are hearing the same prognosis: "Your child will never recover. Be realistic. Autism is an inborn, genetic disease with no effective treatment and no cure."

But there's a difference between then and now. Today, recovery is possible.

Revolutions in Autism

What changed between the 1960s and today? Three revolutions occurred, and all involved parents fighting for their children.

The first successful battle, which began with the publication of my book *Infantile Autism* in 1964, was the fight to end the reign of psychogenic ("blame the mom") psychiatry, which claimed that only psychotherapy could help children with autism. The medical establishment accepted the psychiatrists' approach, and offered no alternative (other than prescriptions for Haldol, an antipsychotic drug). It was parents—armed with the knowledge that no evidence supported psychoanalysis as a treatment for autism—who said, "Enough!" and demanded real treatments for their children.

This led to the second revolution, in which parents learned about, and demanded access to, the remarkably effective teaching techniques (now known as applied behavior analysis, or ABA) pioneered by Ivar Lovaas. Experts initially scoffed at the idea that children with autism who hadn't responded to powerful drugs and years of psychoanalysis could be helped by something as simple and straightforward as behavior modification.

But it is the third parent revolution, which began in the 1960s and now is reaching maturity, that will arm us with the most powerful tools to fight autism. That revolution began when parents started recognizing that the vast majority of children with autism are not programmed from conception to be disabled, but rather are genetically *vulnerable* to environmental insults that trigger their autism, and that when we address these environmental insults and the damage they cause, we can begin to cure "incurable" children and to prevent future children from ever developing autism.

The first signs of this revolution appeared in letters I received, beginning in the '60s and '70s, from parents who reported that a range of seemingly odd and unscientific approaches had helped their children greatly. These approaches included high-dose vitamin B6, yeast-free diets, and gluten- and casein-free diets. At the same time, other parents were reporting that their formerly typical children became autistic, sometimes literally overnight, after receiving vaccines, or that antibiotics, food additives and other chemicals exacerbated their children's autistic symptoms.

I was highly skeptical of these reports at first. As a mainstream psychologist, I initially considered it ludicrous that environmental insults could cause autism, or that a vitamin or a special diet could help with symptoms. But my own research over several decades validated these parents' claims, and I realized that they were far closer to finding real answers about autism, and real treatments for the disorder, than mainstream medicine ever would be. I also realized that in order to benefit today's children, we needed to obtain answers even faster.

Getting Answers

In response, ARI called together a think tank of exceptionally competent and open-minded physicians and scientists interested in identifying safe and effective treatments for autism, and in pinpointing the environmental culprits behind what had by then become an epidemic. We convened the first Defeat Autism Now! (DAN!) conference in Dallas in 1995, inviting approximately 30 physicians and scientists from the United States and Europe with special expertise in autism research and treatment. Several participants, including me, were parents of children with autism, and understood all too well the need for urgency.

The conference was a great success and planted the seeds for the DAN! movement, which now includes many hundreds of physicians and scientists worldwide—many of them also parents of children with autism. These doctors are using chelation therapy, special diets and nutritional supplements to correct the damage done by vaccines, toxins and dietary deficiencies, and the result is nothing short of incredible: Thousands of children are getting better, and many of them are being cured.

The DAN! movement now is so popular that our institute cannot train doctors fast enough to meet the needs of thousands of parents who want to use DAN! approaches to help their children. Typically, these parents aren't hearing about the success of DAN! from their family doctors. Instead they're hearing about it from other parents—a new generation of moms and dads, and sometimes grandmothers and grandfathers—who are leading the way to new understanding and new treatments.

This revolution, like the past two, faces tremendous opposition. Vaccine manufacturers will not willingly admit that their products could be the cause of a devastating epidemic affecting millions of children worldwide. Pharmaceutical companies have a huge stake in making us believe that autism cannot be cured but can only be treated by drugs that suppress symptoms. Traditional doctors, conditioned to think of autism as a genetic disease and to view chelation, nutritional therapies and special diets as "quackery," will try to dissuade parents from exploring such approaches, and will punish the doctors who advocate them.

So once again, it is up to parents to lead the revolution—and we have not one but two battles to fight. The first is the battle to obtain safe, effective, biologically based treatments for our sons and daughters, and to obtain answers about the environmental toxins that have damaged them. The second is the larger battle to create a safer and saner world for all of our children, and generations to come, by removing the environmental insults—mercury, lead, PCBs, pesticides, food dyes and additives, nutrient-stripped food—that are damaging the bodies and minds of entire generations. It will not be an easy fight. But if there is anything we learn as parents of children with autism, it is that the toughest battles are the most important, and they can be won.

AUTHOR

Bernard Rimland, Ph.D., was the director of the Autism Research Institute (ARI) in San Diego, and the founder of the Autism Society of America. He also was the director of ARI's Defeat Autism Now! (DAN!) project, and the co-author (with Stephen M. Edelson) of Recovering Autistic Children. For information about ARI and DAN!, visit www.AutismResearchInstitute.com.

Autism Society of America

7910 Woodmont Avenue, Suite 300
Bethesda, MD 20814-3067

Address Service Requested