

GI and Toxicity Issues in Spectrum Disorders

A.K.A. The Poop and Goop Lecture

Why is it important?

- Digestive disorders were part of the original description of autism
- Digestive disorders can interfere with the learning process (it's hard to learn when your gut hurts)
- Some ASD behaviors are directly related to gut pathology

Why is it important?

- The gut is critical to immune system function
- An imbalanced gut can create compounds that interfere with proper sensory integration
- The gut is the pathway for nutrients

GI tract: the basics

- Stomach: creates an acidic environment, adds pepsin, digests proteins. Also creates intrinsic factor to absorb B12.
- Duodenum: first part of small intestine. Bile from gall bladder and digestive enzymes from pancreas are added.
- Small intestine: absorbs nutrients, plays critical role in total body immunity
- Large intestine: primarily absorbs water from intestinal contents. Majority of flora live here.

Transit Times








- Different foods have different times
- Normal versus ideal

	Normal	Ideal
Stomach	2.5-5 hrs	1-4 hrs
Small Intestine	2.5-3 hrs	2-3 hrs
Colon	30-40 hrs	8-12 hrs
TOTAL	35-48 hrs	11-19 hrs

What is ideal bowel function?

- Should take about one minute
- Stool should be 18-24 inches long and 1.5 inches in diameter (for adults)
- Stool should float
- Should have two to three bowel movements per day
- Should not have gas or excessively foul smell

Bristol Stool Scale

Bristol Stool Chart		
Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

Common GI disorders in ASD

- Intestinal candidiasis
- GERD
- Constipation/Diarrhea/Bloating/Foul Stools
- Eosinophilic Esophagitis
- Encopresis
- IBS/nonspecific abdominal pain
- Pancreatic insufficiency
- Lymphocytic enterocolitis
- Impaired intestinal permeability/food sensitivities

GI disorders--prevalence

- **91% of children on the autism spectrum have GI issues.**
- **25% of siblings of ASD kids have GI issues as well**

McCartney, J of Med Microbiology, 2005; Ashwood, J Clinical Immunology, 2004, 24(6):664; McGinnis, DAN presentation

GI disorders—clinical signs

Obvious signs

- Diarrhea/Constipation
- Bloating/bad gas
- Abdominal pain
- Reflux/emesis
- Food avoidance/“picky eater”
- Weight loss/ failure to thrive
- Fatty/greasy stools
- Large diameter stools

GI disorders—clinical signs

Not so obvious signs

- Rosie cheeks
- Behaviors to put pressure on abdomen
- Smearing of stool/problems with “potty training”
- Sudden especially violent outbursts
- Hyperactivity/inability to focus
- Night time awakening
- Skin rashes
- Allergies/asthma
- Immunologic disorders

GERD/Esoophagitis

- Medical theory of GERD—hiatal hernia with excess acid production. Treat with H2 blockers and PPI's. Problem: need stomach acid to effectively digest proteins and to absorb B12.
- Alternative theory of GERD—inadequate digestion leads to undigested material making it to colon where fermenting (bad) organisms generate gas. This, along with a hiatal hernia, will result in GERD. Treat by improving digestion and gut ecology

GERD/Esophagitis

- 69% of ASD kids have some form of esophagitis
- Esophagitis is usually caused by GERD
- Eosinophilic esophagitis is a special case
 - Eosinophils released in response to parasites or allergens
 - Eosinophilic esophagitis=severe food (or other ingested) sensitivities. Should investigate further.

Pancreatic Insufficiency

- Pancreas function: endocrine vs exocrine
- 75% of ASD kids have some form of pancreatic dysfunction*
- 62% of kids respond favorably to enzyme supplementation (ARI parent ratings)
- Remember—adequate stomach acid is essential for protein digestion. The pancreas makes protein digestive enzymes, but they work in an environment of neutral pH which is not the best for protein digestion

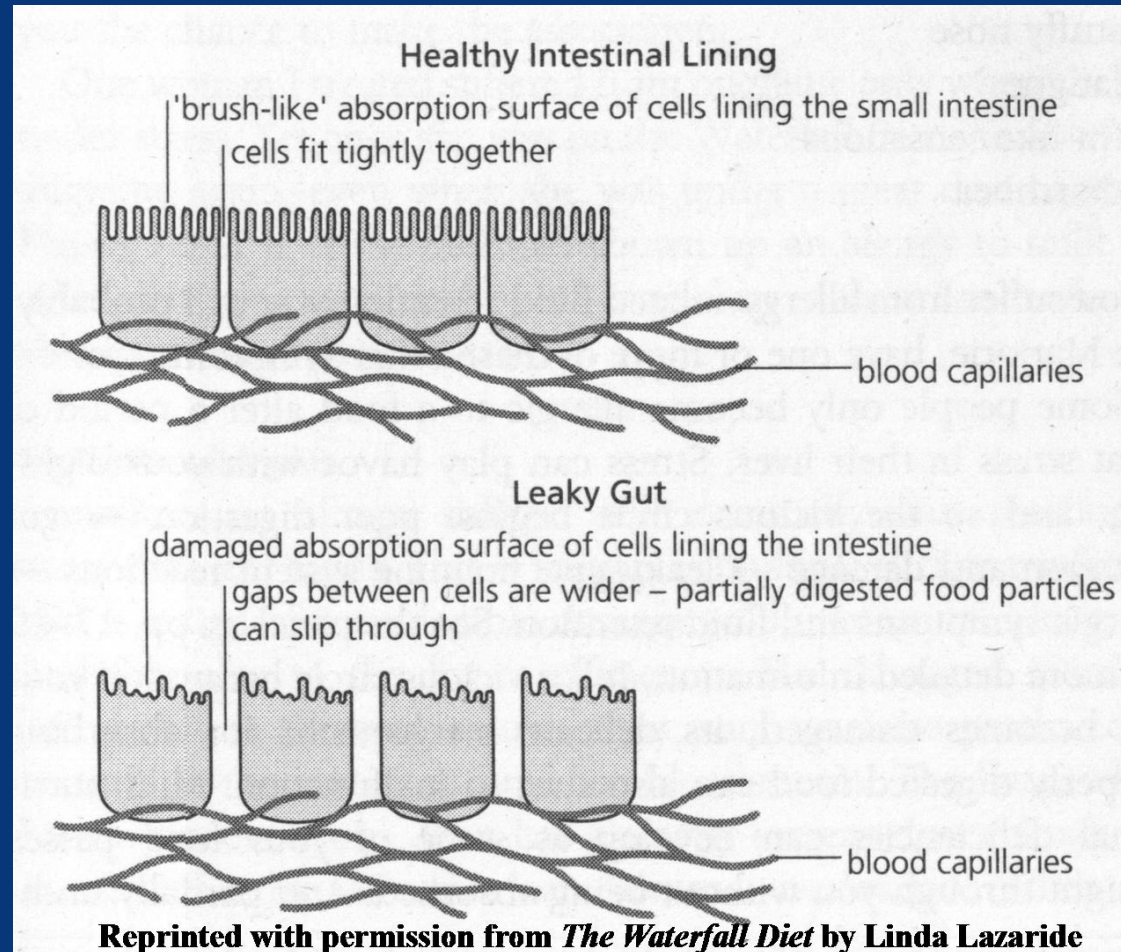
*Horvath, J Pediatrics, 1999, 135(5):559

Intestinal Disorders--IBS

- Frequent diagnosis when no other medical cause can be identified.
- Imbalances of normal intestinal flora can be identified almost 100% of the time
- Small intestine bacterial overgrowth in 78% of people
- Impaired intestinal permeability adds to the problem by creating overactive immune response

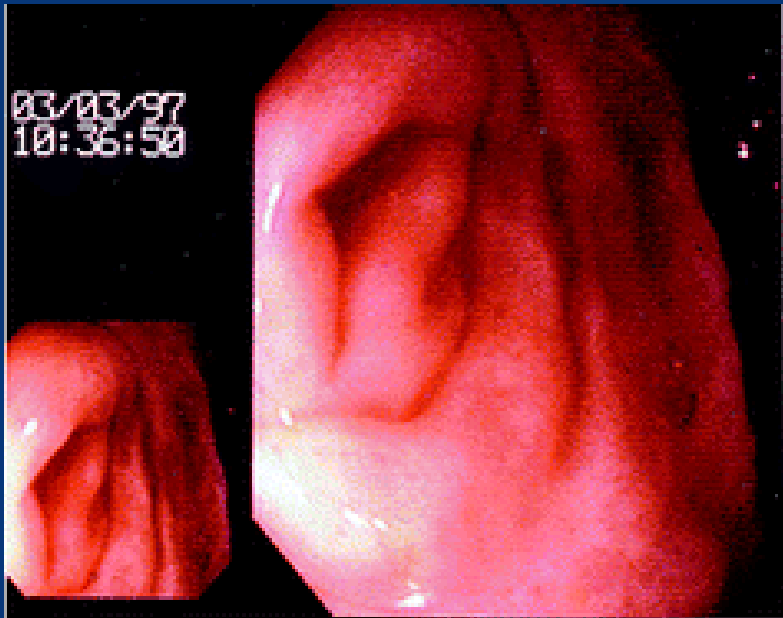
Drisko, et. al., J Amer College Nutr, 25(6):514; Pimentel, et. al., Am J Gastroenterology 95:2503

Intestinal Disorders—Permeability

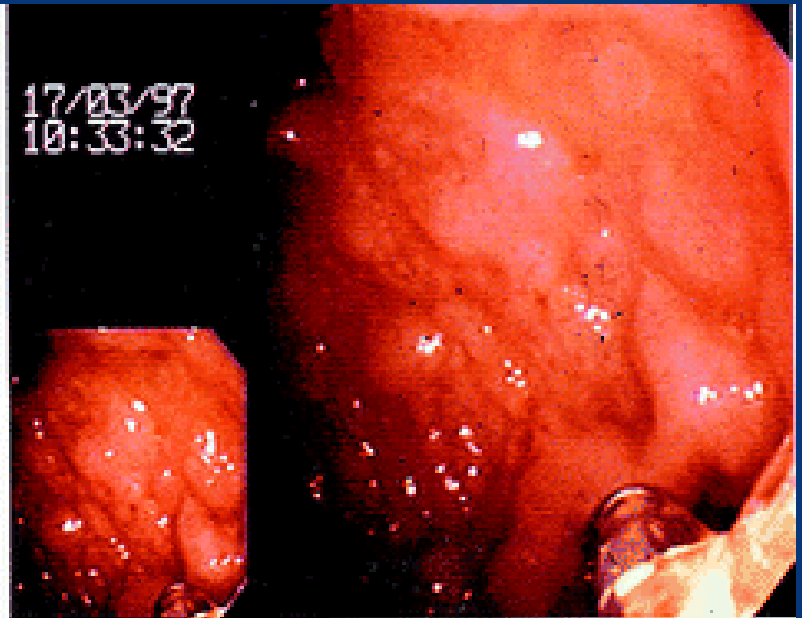


Intestinal Disorders—Diarrhea

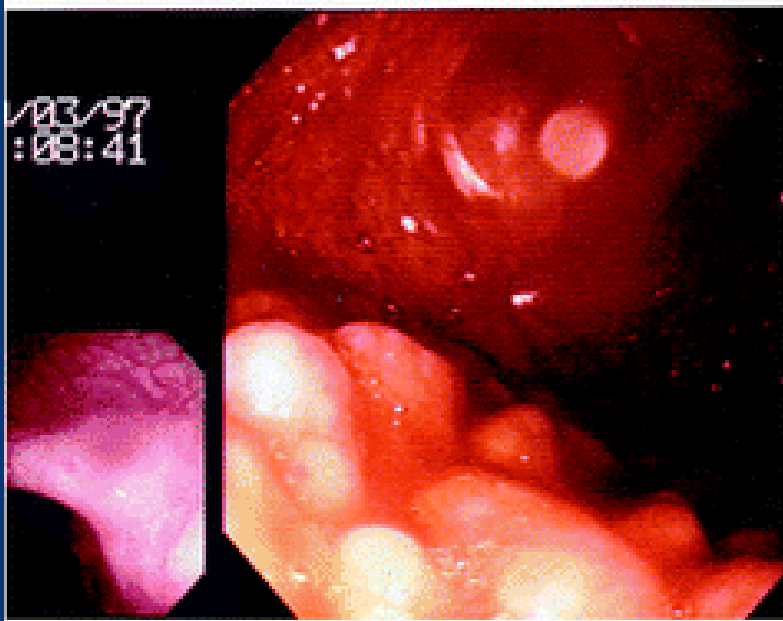
- Must rule out “overflow” diarrhea
- Caused by either irritation to intestinal lining or loss of absorptive capacity
- Importance of the health of the microvilli—any damage will significantly reduce surface area for absorption
- Role of unhealthy bacteria, yeast, parasites
- Lymphocytic nodular enterocolitis



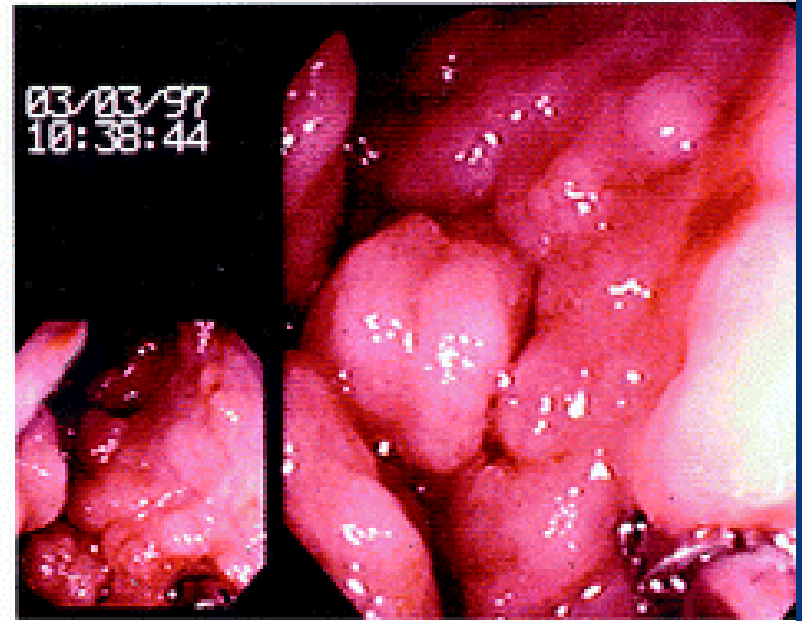
A



B



C



D

Intestinal Disorders--Constipation

- Usually related to colon function
- Colon transit time is the most variable in the digestive tract
- Function of colon is dependent on everything upstream
- Constipating properties of certain foods
- Importance of soluble fiber
- Importance of probiotics
- Mitochondrial dysfunction

Probiotics

- Pro (good) biotic (life form). Includes both beneficial bacteria and yeast
- They out number us
- Essential for normal digestion, absorption of nutrients, immune function, even metabolism
- First line of defense from invading organisms
- 100's of different species
- Starts with birth (*Bifidus infantus*)

Probiotics: C. diff and Fecal Transfer

- Overuse of antibiotics or use of multiple antibiotics can result in overgrowth of Clostridia difficile
- Resistant to most antibiotics
- Causes a colitis
- Eventually becomes resistant to all antibiotics
- 80% cure rate with fecal transfer
- Huge numbers of probiotics involved (1gm of stool = about one trillion organisms)

Probiotics—Why do we need them

- Frequently not colonized properly at birth
- Lack of breast feeding
- Antibiotics disrupt normal populations
- Food is devoid of organisms
- We do not ferment our foods anymore

What is a good probiotic?

- Should have many billions (at least 15-20) of organisms
- Ideally, should have multiple populations of organisms
- Should be purchased fresh
- Refrigerated vs non-refrigerated
- Rotate brands

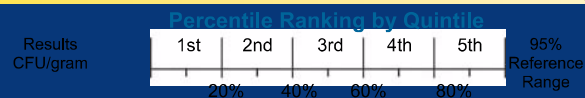
GI tract workup

- Significant issues should be evaluated medically (EGD, colonoscopy, stool culture, C. diff., etc.)
- Food sensitivity (ELISA) testing, including separate celiac testing if indicated
- Urine biochemical markers for bacterial overgrowth
- Comprehensive stool digestive analysis
- PCR analysis for difficult to detect organisms

GI Tract: Workup

2100 Gastrointestinal Function Profile

Methodology: DNA Analysis, GC/MS, Microscopic, Colorimetric, Automated Chemistry, ELISA



Consistency = Formed/Normal

Predominant Bacteria (E+007)

Obligate anaerobes

Organism	Results	1st	2nd	3rd	4th	5th	95% Reference Range
Bacteroides sp.	2.5	1.6				6.7	>= 1.3
Clostridia sp.	2.0	1.5				6.2	>= 1.0
Prevotella sp.	2.1	1.6				6.2	>= 1.1
Fusobacteria sp.	2.6	1.6				7.4	>= 1.1
Streptomyces sp.	1.3 L	1.6				5.8	>= 1.0
Mycoplasma sp.	1.3 L	1.7				6.2	>= 1.2

Facultative anaerobes

Organism	Results	1st	2nd	3rd	4th	5th	95% Reference Range
Lactobacillus sp.	1.3 L	1.8				7.8	>= 1.2
Bifidobacter sp.	2.5	2.3				7.6	>= 1.8

Obligate aerobes

Organism	Results	1st	2nd	3rd	4th	5th	95% Reference Range
Escherichia coli	2.8	1.7				7.7	>= 1.1

Opportunistic Bacteria

Klebsiella sp.	2.8E+008 H	<=1.0E+005
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Units and Reference Ranges

Organisms are detected by DNA analysis. One colony forming unit (CFU) is equivalent to one bacterium. Each genome detected represents one cell, or one CFU. Results are expressed in scientific notation, so an organism reported as 2.5 E7 CFU/gram is read as 25 million colony forming units per gram of feces. The cutoff for significance of Opportunistic Bacteria has been set at 1.0E+005 (100,000). These are levels above which clinically significant growth may be present. Rather than reporting semi-quantitative +1 to +4 levels, the new methodology provides full quantitative analysis.

Predominant Bacteria play major roles in health. They provide colonization resistance against potentially pathogenic organisms, aid in digestion and absorption, produce vitamins and SCFA's, and stimulate the GI immune system. DNA probes allow detection of multiple species (sp.) within a genus, so the genera that are reported cover many species.

Opportunistic Bacteria may cause symptoms and be associated with disease. They can affect digestion and absorption, nutrient production, pH and immune state. Antibiotic sensitivity tests will be performed on all opportunistic bacteria found, although clinical history is usually considered to determine treatment since the organisms are not generally considered to be pathogens.

GI Tract: Workup

Microbiology

Bacteriology

12. Beneficial Bacteria

Lactobacillus species
Escherichia coli
Bifidobacterium

*NG	
*NG	
	(2+)

13. Additional Bacteria

gamma haemolytic Streptococcus

NP	(2+)
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14. Mycology

Candida albicans
Candida krusei
Candida glabrata (T. glabrata)

PP	(2+)
PP	(4+)
PP	(4+)

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathological significance should be based upon clinical symptoms and reproducibility of bacterial recovery.

*NG
*NG

No Growth

NP

Non-Pathogen

PP

Potential Pathogen

P

Pathogen

Lab Comments

All Yeast Sensitivities.

Treatment—the three R's

- Remove the bad stuff
- Repair the damage
- Replace the good stuff

Treatment—Remove

- Remove offending foods
- Stop feeding fermenting organisms (sugars)
- Avoid antibiotics
- Species specific anti-microbial treatment
- Work with your doctor to get off medications that might interfere with GI function

Treatment—Remove: Biofilms

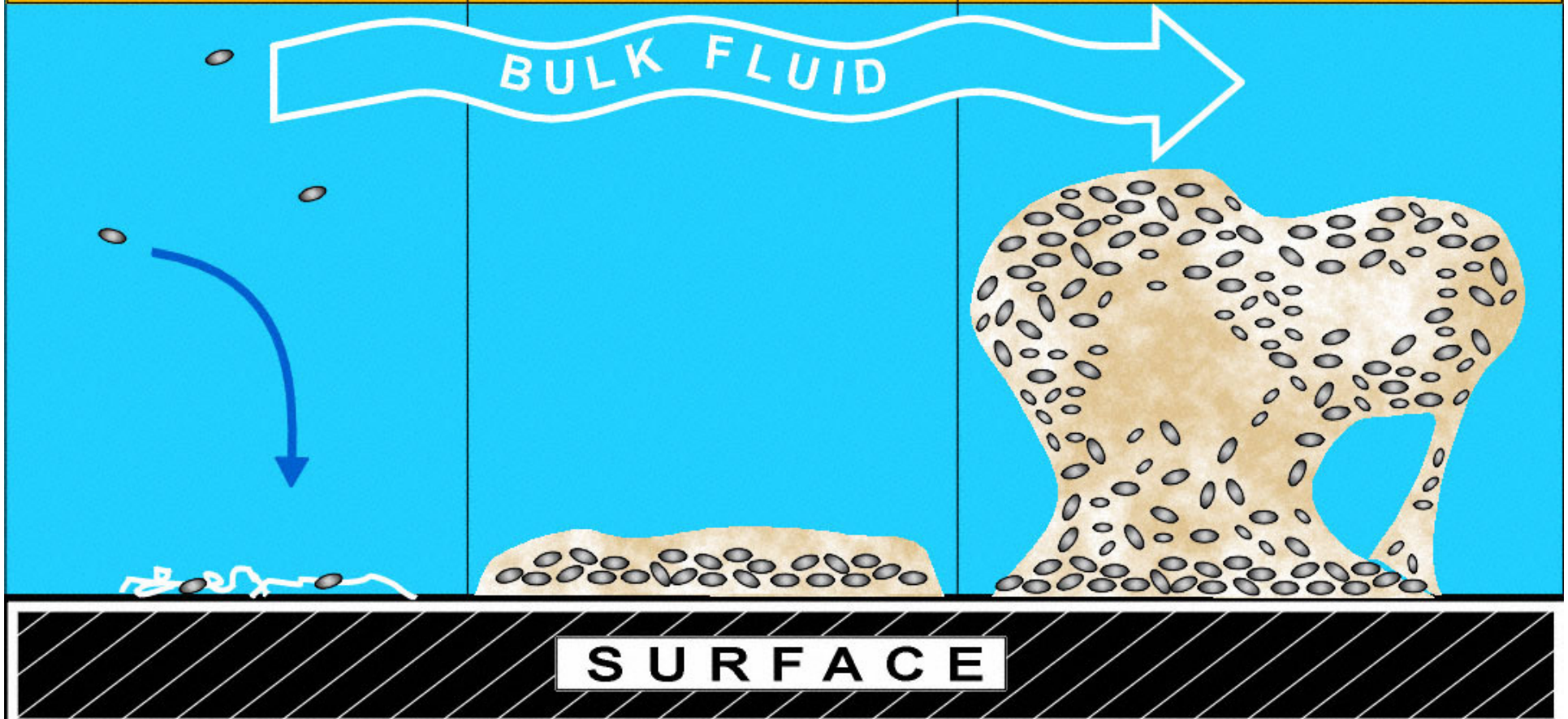
- Many organisms will form biofilms
- Consists of organisms binding together with with both protein bonds and calcium bonds
- Biofilm protects organisms from immune response and antimicrobial agents
- Treatment involves breaking protein bonds with enzymes and breaking calcium bonds with EDTA

Biofilm formation:

Attachment

Colonization

Growth



Treatment—Repair

- Glutamine
- Curcumin extracts
- Gamma Oryzanol
- N-acetyl glucosamine
- Zinc
- Histidine
- Transfer factor/IP-6/other immune modulators
- Pre and Probiotics
- *Saccharomyces boulardii*
- Carnitine/ribose

Treatment—Replace

- Digestive enzymes
- Probiotics
- Amino acids
- Fermented foods (bodyecology.com)
- Prebiotics including inulin and soluble fiber
- Apple cider vinegar
- Good quality, nutritious, organic food

GI tract—wrap up

- GI dysfunction very common in ASD kids
- Plays critical role in nutrient delivery, metabolism, brain and immune function
- One of the primary modes of detoxification
- Traditional medical approach tends to miss many of the functional issues
- Solutions exist for many, if not all, GI issues

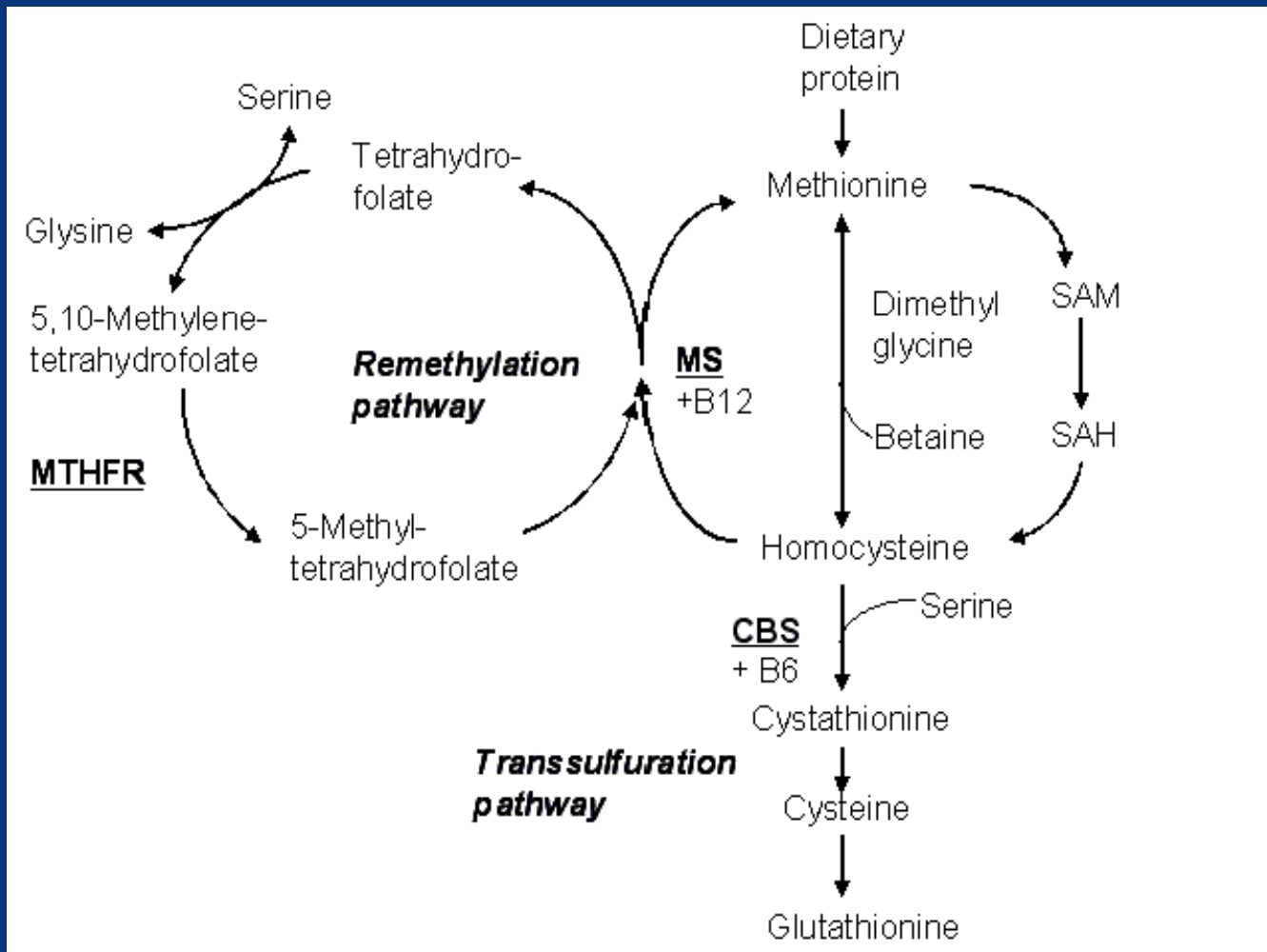
Toxicity—Why is it important?

- Children with ASD have impaired detox mechanisms
- Toxicity contribute to inflammation and oxidative induced brain injury
- Changes in pesticide types and increased use of plastics have worsened toxicity
- Of the 80,000 chemicals in common use, we suspect 1000, we know something about 100, and about 10 are well studied
- Only a small minority of disease is solely genetic, the vast majority is environmental=toxin exposure

Types of Impaired Detox in ASD

- Kids with ASD are known to have decreased levels of glutathione.
- Variations in PON-1 gene increase susceptibility to pesticides
- Altered methylation pathways (MTHFR, MTRR)
- Impaired mitochondrial function
- Certain genetic disorders make a child more susceptible to heavy metals (ALAD and lead)

Types of Impaired Detox in ASD



Published Toxicants Associated With ASD

- Mercury
- Lead
- Cadmium
- Nickel
- Trichloroethylene
- Tin
- PCBs
- Vinyl chloride
- Phthalates
- Diesel particulate matter
- Solvents
- Pesticides
- Chemical exposure in parents before pregnancy
- Living close to a U.S. EPA Superfund site

Sources of Toxins—Prenatal

- Dietary (seafood consumption)
- Thimerosal containing vaccines (flu, Rhogam)
- Dental amalgams
- Smoking (cadmium)
- Alcohol use
- Lead stored in bone
- Mercury and other metals stored in tissue
- Occupational exposures

Sources of Toxins—Postnatal

- Toys (China)
- Mercury (flu) and aluminum from vaccines
- Environmental (agriculture, industry, aerial spraying)
- Dietary sources (including packaging and prep)
- Household (lead paint before 1978), cribs
- Amalgams
- Water

The Links to ASD—Some Evidence

- Mothers living within 500 m of fields where organochlorine pesticides were used—6x more likely to have a child on the spectrum*
- For every 1000 lbs of mercury released into the environment, there was a 63% increase in ASD rates**
- Prenatal tobacco use and lead levels caused a 2.5 fold and 4.1 fold increased risk of having a child on the spectrum***

*Roberts, et al, Environ Health Perspect 2007, 115:1482; **Palmer, et al, Health and Place, 2006, 12:203; ***Braun, et al, Environ Health Perspect, 2006, 114:1904

A special word about GMO foods

GMO = genetically modified organism

Genes for naturally occurring pesticides or compounds that make plants resistant to herbicides are spliced into the genome of the food. Soybeans and corn are notorious for this.

With GMO foods—the pesticide is in the food; you can not wash it off

Toxicity—The Workup

- Provoked urine challenge
- Urine porphyrin testing
- Hair Analysis
- Glutathione/Cysteine/Sulfate levels
- Oxidative stress markers
- Mitochondrial stress markers
- Testing for genetic markers (MTHFR, MTRR, PON-1, CBS, etc.)
- History

The 3 R's of Toxicity—Remove

- Optimally, mothers should detox before pregnancy
- Eat organic foods—especially chicken (arsenic), berries, and things that cannot be peeled
- Avoid seafood
- Avoid plastics
- Avoid use of things with Teflon, SilverStone, Stainmaster, Gore-Tex, Scotchgard—all have PFCs

The 3 R's of Toxicity—Remove

- Dishes or cups should be glass (ceramic if you know there is no heavy metal in the glazes)
- Drink purified water—at least filtered: R.O. or distilled water are better (minerals)
- Use air purifiers
- Use mercury free dental materials
- If you are using vaccines, make sure they are Thimerosal and aluminum free.
- Avoid GMO foods (especially soy and corn—many others)

The 3 R's of Toxicity—Remove

- Chelation therapy—topical, oral, suppository, IV. Use chelator specific to child's toxicity
- Far Infra-red saunas—any sweating will help detox. FIR saunas result in sweat with much higher concentrations of toxins such as heavy metals
- Support detox pathways
- Move

The 3 R's of Toxicity—Repair/Rebuild

- Increase glutathione—methylB12, methyl folate, glutathione, N-acetylcysteine, alpha lipoic acid, vitamins C and E.
- Anti-inflammatories: curcumin, low dose naltrexone, pycnogenols, omega 3 fatty acids
- Epsom salt baths (magnesium sulfate)
- Herbal supports for liver
- Support proper digestive elimination

Top Ten List for Avoiding Toxicity

- 1) Buy non-toxic products for your home
- 2) Keep indoor environments healthy
- 3) Don't reheat or microwave foods in plastic
- 4) Eat lower on the food chain
- 5) Buy organic and local
- 6) Dispose of household toxic products properly
- 7) Become involved
- 8) Educate yourself/read labels
- 9) Involve your neighbors/find green alternatives
- 10) Take political action—let your legislator know your concerns.

Resources

Nontoxic products:

www.iceh.org

www.checnet.org

<http://householdproducts.nlm.nih.gov>

“Safe” plastics

www.ecologycenter.org/ptf/toxins.html

Safe cosmetics

www.safecosmetics.org

www.cosemeticsdatabase.com

Pesticides

www.sustainabletable.org

www.checnet.org

Resources

Pesticides (cont'd)

www.beyondpesticides.org

www.pesticides.org

www.epa.gov/pesticides/factsheets/npic.htm

General Information

www.healthandenvironment.org/initiatives/childrens_health/columns_facts