



dialog

Doctor's Data, Inc. (DDI), the premier clinical laboratory with over 30 years' experience, provides specialty testing to healthcare practitioners around the world. A specialist and pioneer in essential and toxic elemental testing of multiple human tissues, the laboratory offers a wide array of functional testing. DDI's tests are utilized in the assessment, detection, prevention, and treatment of heavy metal burden, nutritional deficiencies, gastro-intestinal function, hepatic detoxification, metabolic abnormalities, and diseases of environmental origin.

DDI is a licensed CLIA laboratory with appropriate state certifications and participates in numerous quality assurance/proficiency testing programs including the College of American Pathology, New York State DOH and Le Centre de Toxicologie du Quebec.

We are pleased to reintroduce our periodical "dialog" which is designed to facilitate an interactive flow of information between physicians and our lab. At the back of this issue is a "Q&A" section. Should you have any questions about our services, please contact us at tech?@doctorsdata.com. Selected questions and answers will be presented in future issues of "dialog."

Arsenic in Drinking Water

by Dean Bass, Ph.D.
Technical Director, Doctor's Data, Inc.

The EPA has decided to lower the allowable level of arsenic in drinking water from 50 ppb to 10 ppb by 2006. The 50 ppb standard dates back to 1943 and is generally regarded as inadequate to protect health. The move has been proposed for some time and has been continually delayed for political and economic reasons. New standards ranging from 3 to 20 ppb had been considered. Both the European Union (EU) and the World Health Organization (WHO) have standards for arsenic in drinking water set at 10 ppb.

Arsenic can be introduced in the environment in pesticides and in the glass and electronics industries. But, it is also naturally occurring in the earth's crust which may result in high levels of arsenic in drinking water. As such, arsenic levels are often elevated in selected locations throughout the US and the World. Bangladesh

and West Bengal, India have had significant problems from high levels of arsenic in the water supply. Elevated arsenic levels in drinking water have been associated with bladder, skin and lung cancers, as well as with its non-carcinogenic effects as seen in pigmentation changes, skin lesions and peripheral vascular disease. The economy and poor nutrition of the region exacerbate the problem. More information on this crisis is available at www.bicn.com/acic. Areas in the US also have dangerous levels of arsenic. While the EPA allows municipalities time to set up systems to comply

Because DDI uses state-of-the-art ICP-MS analysis, it has superior detection limits

with the upcoming lowering of the arsenic standard, Doctor's Data, Inc. (DDI) now reports unacceptable levels of arsenic as greater than 10 ppb. This is consistent with the EU and WHO and the plans of the US EPA. In addition, DDI will also indicate caution levels down to 2 ppb where there is a 1 in 10,000 cancer risk. Because DDI uses state-of-the-art ICP-MS analysis, it has superior detection limits to many environmental labs, which

need only indicate whether drinking water arsenic levels exceed 50 ppb.

Drinking water should be tested under the following situations:

- Clinical tests show unknown exposure to toxic elements
- Symptoms of metal toxicity (see your doctor)
- New well
- New house
- Reports of water problems in your area
- Old house
- New water filtration system
- New water source

For more information on arsenic in drinking water or to order a drinking water test kit for arsenic and 16 other toxic elements regulated by the EPA, please visit www.doctorsdata.com. ■

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Attention-Deficit Disorder (ADD)

by Ron Parks, M.D., M.P.H.

Attention-deficit/hyperactivity disorder (ADHD), also commonly referred to as Attention-deficit disorder (ADD), occurs in about 4 to 5% of the population. There are three subtypes according to what symptoms predominate: (1) inattentive, (2) hyperactivity-impulsivity and (3) the combination of 1 & 2 (more common in adults). The age of recognition in adults is around forty, though it must be present to some degree since age seven or younger for diagnosis. After age twelve, 50 to 60% of children will continue with ADD symptoms into adulthood—usually of the inattentive type—as difficulties with organizing, sustaining attention, internal restlessness, distractibility, finishing tasks, procrastination, losing things, forgetfulness and making mistakes. Difficulties relaxing quietly may relate to substance abuse in adolescence or adults.

ADD becomes a disorder in adults when symptoms cause significant impairment over time in important areas of life as work, family life and social activity. This can contribute to substance abuse, ill health from chronically over extending oneself or not getting adequate sleep or relaxation. ADD passes from parent to child as a common inherited condition.

The concept of “total load” from environmental medicine is helpful in recognizing, removing or reducing key factors that can either perpetuate ADD or make it worse. These may

include—sensitivities, allergies, exposures to chemicals, foods, inhalants, infections, psychosocial stresses, electromagnetic fields and/or genetic influences. There are several valuable lab tests which can elucidate some of these factors, aimed at reducing or eliminating ADD symptoms.

Evaluating digestive factor or disturbance in the GI tract can uncover contributors to ADD symptoms. Doing a Comprehensive Stool Analysis (“CSA”) and Parasitology can uncover the presence of potentially pathogenic bacteria species, yeast and parasites, or inadequate levels of necessary healthy bacterial flora. It can also uncover other infectious pathogens by EIA testing as—*Campylobacter*, *Enterohemorrhagic E. Coli*, *Giardia lamblia* and *Cryptosporidium*. This test also will uncover defects in digestion and absorption of nutrients by the measurements of chymotrypsin, triglycerides, muscle and vegetable fibers, cholesterol, carbohydrates and steatocrit %.

The CSA also can guide the clinician in his treatment of ADD with its indices and markers of: elimination efficiency of undigested food residues and toxins, intestinal immune dysfunction (fecal sIgA), inflammation (lysozyme and lactoferrin levels) and impairments of intestinal health (presence of RBC's, WBC's, mucus, occult blood, abnormal short chain fatty acid patterns and pH of stool).

Once uncovered, contributors to ADD can be corrected as—maldigestion, inadequate absorption/assimilation of critical nutrients as minerals, amino acids, vitamin cofactors and essential fatty acids. A Lactulose/Mannitol Test looks for evidence of increased intestinal permeability problems which allow the entry of antigens into the body with resulting immune antibody responses and often-related systemic illness and allergies. High percent of the larger Lactulose molecule in the urine indicates Intestinal Permeability, while low recovery of the smaller Mannitol molecules in urine indicates Malabsorption. Once increased intestinal permeability is identified, underlying causes can be eliminated and types of treatments can be better selected.

Random urine D-Glucaric and Mercapturic acids provide useful information about toxic chemical, pesticide exposure (xenobiotics) and of adequate liver enzymatic detoxification in the individual with ADD. Hair element analysis is a good screening test for excess, deficiency or maldistribution of essential and nonessential minerals or toxic metals—as mercury, lead, cadmium and arsenic. Urine elements analysis by ICP-MS at Doctor's Data, Inc. (DDI) can confirm suspected accumulations of toxic metals in the body. A provocation test with a chelating agent as DMSA or DMPS and a 6-hour urine elements test follow a baseline

24-hour urine elements test. DDI's Fecal Metal test does evaluation of environmental exposure, accumulation and of the body's natural toxic metal detoxification.

A 24-hour urine for Amino acid analysis (Plasma used when compliance or urine collection is difficult) is one of the most valuable tests in uncovering some of the root contributors to ADD. It can detect dietary protein inadequacies, gastrointestinal dysfunction, nutritional deficiencies of vitamins and minerals, renal and hepatic dysfunction, inherent disorders in amino acid metabolism and more. Nutritionally oriented clinicians have found that supplementation with the precursor amino acids of neurotransmitters such as tyrosine, glutamine, 5-HTP, L-tryptophan, and specific mineral and vitamin cofactors are beneficial in the treatment of ADD, depression and anxiety. This is possibly a safer choice than conventional use of psycho-stimulants as Ritalin or Adderall, or antidepressants as Wellbutrin.

Testing for RBC elements and fatty acids analysis are important guides for correcting mineral or fatty acid imbalance often found in ADD. Other natural approaches are recognizing and treating allergies; improving nutrition as avoiding additives, chemicals and refined sugars; ADD coaching; behavioral cognitive therapies to help modify dysfunctional patterns

and to help with focusing; family therapy and EEG Biofeedback. For guidance in doing or interpreting any of the testing discussed above, call and consult with one of the knowledgeable and experienced DDI consultants. ■

Ronald R. Parks, M.D., M.P.H. is a clinical consultant with Doctor's Data, Inc. and is specialty trained in Psychiatry, Internal, Family & Preventive Medicine with a background in nutrition and other natural healing arts. He acts as a bridge between the best of conventional Western medicine and the innovative approaches of Integrative Medicine and Psychiatry. Dr. Parks received his M.D. from the University of Maryland, a Master's Degree in Public Health and Health Services Research from UCLA, specialty trained in Internal Medicine at George Washington University, Preventive Medicine at UCLA and Psychiatry at the University of Maryland. Dr. Parks served as Assistant Professor at The Albany and University of Miami Medical Schools, and as Director of the Center for Preventive and Nutritional Health Care in Baltimore, Maryland. He is currently Director of Integrative Medicine and Psychiatry services in Asheville, North Carolina.



Digestive Testing

by Marty Lee, Ph.D.

Since Dr. Jonathan Wright first popularized digestive analyses in the 1980's, laboratory testing has greatly evolved. In earlier years, a doctor ordered a test to confirm something already suspected and made use of it as a motivational tool for patients and/or as a general screen to see if the patient had any "positive" findings. However, in today's world of skyrocketing medical costs and diminished reimbursements, a test has to meet stricter criteria before doctors order it and patients and third party payers pay for it. Most importantly, the results must provide specific cost-effective and beneficial treatment options for the patient which otherwise would not be known.

Digestive/stool analysis meets these strict standards. Its unquestionable value to clinicians is based on the awareness that digestive and nutritional disturbances are involved in virtually every chronic medical condition of Western civilization—hypertension, heart disease, cancer, arthritis and rheumatoid conditions, food allergies, migraine headaches, asthma and more. In these, as in most illnesses, good nutrition and a well functioning digestive system play an essential role in prevention, health maintenance and treatment.

It is not sufficient to simply tell patients that eating well will improve their conditions. In treating patients with specific

complaints, it is essential to determine exactly what is abnormal in their nutrition and digestion and how this may be affecting them. Digestive analyses give direction and guidance for specific digestive treatments and remedies. A comprehensive stool analysis (CSA), as performed by Doctor's Data, Inc. (DDI), will look at the possibility of:

1. Parasite infestation
2. Yeast overgrowth
3. Imbalanced bacterial flora
4. Inadequate fat and protein digestion
5. Malabsorption
6. Abnormalities of fiber digestion
7. Status of immune function in the digestive tract

All of these abnormalities are readily treatable — either with antibiotics, antifungals, herbs, and/or natural products. Many authorities consider the first three microbial abnormalities in the list above to be the basis of dysbiosis (unhealthy gut flora) or eubiosis (healthy gut flora). Treatments for all of these conditions are readily available. It would be unreasonable to treat patients as if all of the above were going on at once, shot gunning them with more herbs, supplements and antibiotics than they may need, want or can afford. Each patient is unique and can benefit from an individualized lab based treatment program.

A comprehensive stool analysis can play a crucial role in assisting a physician in

helping patients with a wide variety of chronic conditions. Doctor's Data designed the CSA to have the broadest and most useful indicators of nutritional and digestive health. The team of laboratory professionals at Doctor's Data is dedicated to helping you and your patients in every way possible.

Moreover, I want to assure you, and offer you my pledge that I am here to listen to you, to answer any questions you may have, and to help in any way possible. If I can be of assistance, please do not hesitate to call Doctor's Data and ask for me (1-800-323-2784), or e-mail me at Mlee@doctorsdata.com. ■

Dr. Marty Lee is the former CEO and Laboratory Director of Great Smokies Diagnostic Laboratory. After receiving his Ph.D. in biochemistry and microbiology from Rutgers University, Dr. Lee worked for 15 years developing kits, reagents and instruments for the clinical lab. Dr. Lee was a senior researcher at Technicon Corp, receiving four patents on his work, and was Director of Research at Coulter Diagnostics. After years of rapid advancement and achievement, Dr. Lee desired to work more closely with physicians and patients.

Opening a clinical lab dedicated to digestive analysis, Dr. Lee achieved prominence for his efforts to promote the significance of parasitology and high quality laboratory services in diagnosis and treatment of chronic diseases. In becoming the laboratory director at

Heavy Metal Poisoning Diagnosis and Treatment

by David W. Quig, Ph.D.
V.P. Scientific Support, Doctor's Data, Inc.

Great Smokies Diagnostic Laboratory in 1989, Dr. Lee brought his skills in laboratory science and management to bear on the broad array of lab services in complementary medicine and chronic illness.

In 1998, Dr. Lee retired from Great Smokies Lab and moved to Israel where he has studied Torah (Bible). In 2001, Dr. Lee joined the team of professionals at Doctor's Data, helping extend the DDI tradition of excellence in trace minerals and amino acids to the variety of digestive analyses.

Environmental pollution is a growing problem which makes all of us vulnerable to chronic, low level exposure to toxic metals in our air, water, food and dental restorations. An example would be the legal and common practice of dispersing industrial toxic wastes that contain heavy metals found in the liquid fertilizers used to support crops and grazing lands. The EPA estimates that annually approximately 58 tons of mercury is released into the atmosphere. Much of this mercury will ultimately become incorporated into the aquatic food chain. The relatively slow accumulation of toxic metals in the body is associated with diverse and rather nonspecific symptoms. The overt expression of associated chronic disease is often not realized until later in life. The most commonly encountered toxic metals, lead (Pb), mercury (Hg), arsenic (As) and cadmium (Cd) are neurotoxic, nephrotoxic and associated with cardiovascular disease, immune dysregulation and osteomalacia. In the cardiovascular system the metals impair endothelial function and stimulate the oxidation of atherogenic LDL-apoB. A recent study revealed a 22,000-X enrichment of cardiac tissue Hg levels in patients with idiopathic dilated cardiomyopathy. In the central nervous system, Pb and Hg

disrupt microtubule assembly (cytoskeletal), neurotransmitter metabolism and electrolyte homeostasis. In general, the transition metals promote excessive production of lipid peroxides/hydroxyl radicals, inhibit antioxidative enzymes, and inhibit a plethora of enzymes by virtue of their high affinity for free sulfhydryl groups (eg. creatinine kinase, Na/K ATPase). The metals deplete intracellular glutathione (GSH), and also inhibit enzymes involved in the synthesis and metabolism of this important antioxidant and metal-conjugating peptide. The body adapts to exposure to the metals by upregulating the synthesis and metabolism of GSH, but the availability of cysteine is the rate limiting factor. A second adaptive response to metals is the upregulation of metallothionein, which is a cysteine-rich metal binding protein. Indirect evidence to date suggests that abnormal metabolism of metallothionein may be responsible for the large intra-individual variability in susceptibility to metal toxicity. This is most apparent in young patients, who have been diagnosed with ADD/ADHD and autism.

The accumulation of toxic metals is also associated with depletion of specific amino acids that are involved in endogenous detoxification processes, as well as essential

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Heavy Metal Poisoning

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elements such as selenium (stable adduct formation), zinc, copper, molybdenum and magnesium. Metal-induced immunosuppression is also commonly associated with gastrointestinal dysfunction which impedes the assimilation of nutrients in general. Hence, a vicious cycle of poor nutritional status, immunosuppression and poor absorption further decreases the capacity for endogenous detoxification. The levels of metals in blood and urine (random specimen) are only reflective of recent exposure and do not accurately reflect body burden. To assess body burden one typically starts with hair elemental analysis followed by confirmation by means of biliary/fecal metal analysis, or urinalysis after administration of a specific chelating agent. Heavy metal detoxification typically requires the use of pharmaceutical chelating agents such as EDTA, DMPS or DMSA. However, it is difficult to achieve safe and efficient metal detoxification without maintaining optimal levels of essential elements (packed red blood cell or white cells) and amino acids (plasma/urine). It is clear that there exists a dynamic interplay between toxic metal exposure and nutritional status. Early detection of toxic

metal accumulation, removal from the exposure, and appropriate nutritional support of endogenous detoxification processes are paramount for the mitigation of the chronic adverse health effects that are associated with the toxic metals to which we are exposed. ■

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Minerals, Toxic Metals and Behavior

by David W. Quig, Ph.D.

V.P. Scientific Support, Doctor's Data, Inc.



International studies report a broad range of estimates for the prevalence of childhood mental health problems. Evidence suggests that about 20% of children and adolescents suffer from one or more psychological disorders, which may significantly impair day-to-day functioning. Recent research also indicates that behavioral problems in early childhood can predict psychiatric disorders later in life. Children who were impulsive, restless and distractible at age three were found more likely to be suicidal, antisocial and engage in criminal behavior by age 21.

Despite the importance of these behavioral and developmental problems, the etiology of childhood psychiatric disorders remains poorly understood. Doctor's Data, Inc. (DDI) has recently performed studies to address the influence of abnormal levels of toxic and essential elements on children's behavioral and intellectual development, and on Autism Spectrum Disorder. In collaboration with Dr. James LeClair, University of Victoria, DDI examined the relationship between hair element status and problem behavior in 237 children (grades K-4) in Victoria, BC.¹ The study classified children based on behavioral status using the Walker Problem Behavior Identification test. Using logistic regression analysis,

Dr. Quig received his Masters degree in Human Nutrition from Virginia Tech, Blacksburg, VA, in 1980 and his Ph.D. in Nutritional Bio-chemistry from the University of Illinois, Champaign, IL, in 1984. For the subsequent 12 years he performed and published basic biomedical research as a Research Associate at Cornell University and as a Senior Research Pharmacologist at the Burroughs Wellcome Co., Research Triangle Park, NC.

Dr. Quig is Vice President, Scientific Support for Doctor's Data, Inc. where he continues to design and implement research and laboratory tests pertaining to the dynamic interplay between nutrition, metabolism and environmental toxins. Dr. Quig also consults with physicians about test results and chelation protocols, and presents lectures related to metal toxicity and nutrition at national and international medical conferences on a regular basis.

Q&A

Ask the DDI Consultant

low calcium (Ca) levels were associated with acting out, withdrawal, distractibility and total scores. Distractibility (attention deficit) was the behavior most highly correlated with abnormal hair element levels. There were statistically significant associations with low Ca, high manganese (Mn) and high cadmium (Cd). Although an essential element, excess Mn is well documented to be a potent neurotoxin that adversely affects dopaminergic neurons and dopamine metabolism in specific regions of the brain. Further, Mn uptake is enhanced by low Ca intake. This poses a challenge for dairy product-restricted children, and for infants who consume soy based infant formulas that are absurdly high in Mn. The high Cd levels in the current study¹ are consistent with other reports in which elevated hair Cd was also observed for children with learning disabilities², dyslexia³, delinquency, schizophrenia, high anxiety⁴ and low intelligence scores⁵. Treatment/follow-up studies were not performed in the current study, but diet/nutritional intervention for calcium insufficiency and EDTA suppositories—for chelation of Mn and Cd—are logical therapeutic approaches for afflicted children.

In studies of autistic children (n=221), post-challenge urine mercury levels were significantly higher than in non-autistic controls. In a separate study, fecal levels of cadmium, lead, antimony, uranium and

bismuth were significantly higher (p<0.05) for autistic (n=53) vs non-autistic controls (n=100). Preliminary data suggest that the concomitant use of DMSA and lipoic acid appear to enhance the biliary/fecal excretion of metals in autistic children. Collectively, the results of these studies are highly suggestive of a role, if not causal, of toxic metals in neurological/cognitive deficits and aberrant behavior in children. Therefore, it seems prudent to take measures, as early as possible, to ensure adequate essential element intake and minimize exposure to neurotoxic metals. Further, the assessment of retention and the initiation of safe and effective metal detoxification therapy may potentially mitigate progressive and potentially irreversible neurological disorders in children. ■

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QUESTION

Of what value are creatinine levels in interpreting urine elements?

ANSWER by Karen Urek, DDI Vice President of Operations

Explanation of measurement units for urine element analysis: When measuring any substance in urine one must account for the relative amount of water excreted by the individual. The concentration of a substance can vary over a fifteen-fold range depending on the water content. The two most commonly utilized methods to account for this variability are; 1) 24-hour urine collection (µg/24 hours) or 2) ratio concentration of substance to that of creatinine (µg/g creatinine).

When doing a 24-hour urine collection, all urine during a 24-hour period must be collected and accounted for. The total volume is multiplied by the measured concentration. Reference ranges have been determined based on performing a complete 24-hour collection. If the collection is not done correctly, or the volume of urine is not measured correctly, then the results are not valid.

Creatinine is excreted at a constant rate and is relatively reproducible in a given individual. The concentration of creatinine is an indicator of the dilution or water content of the urine. Therefore, the ratio of the concentration of the element to that of creatinine is advocated as a means to provide an accurate estimate of the total urinary excretion of the substance.

DDI will provide you with both measurement units when a 24-hour urine collection is done. The results from these two methods of calculating the concentration of an element in urine should be comparable within their respective reference ranges. Extreme differences may be an indication of an improperly collected urine sample. If timed or random urine is submitted, the result will be reported using the creatinine method only.

When a random or timed urine collection is reported, the concentration of creatinine is reported as mg/dL. The reference range is only an indicator of the levels of creatinine normally observed when a normal amount of liquid has been consumed by the patient (1000ml – 2000ml/day). If a patient consumes less liquid, the creatinine would be expected to be high (more concentrated urine). If the patient consumes more liquid, the creatinine would be expected to be low (more dilute urine). Therefore, this creatinine result generally does not represent renal problems; it primarily is an indicator of urine dilution.

When a 24-hour collection is provided, the creatinine result is calculated using the 24-hour volume. The result is the amount of creatinine excreted in a 24-hour period and when there is normal renal filtration taking place, this value should be within an expected range. This then becomes a meaningful result to assess renal function.

QUESTION

"I did a provocation test with I.V. DMPS on a patient, followed by a six hour urine element analysis for toxic metals and essential elements, and found mercury elevated to 20 µg/mg Creatinine, with high copper, and low magnesium. After 5 rounds of oral chelation with DMSA 500 mg three times per day for three days and off for eleven days, I repeated an I.V. DMPS provocation test with a six hour urine element analysis and found mercury even higher at 40 µg/mg Creatinine, and continued high copper and low magnesium levels. Why wasn't the mercury level reduced and what does the high copper and low magnesium mean?"

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ANSWER by Ron Parks, M.D., DDI Clinical Consultant

The first DMPS provocation test showed increased body stores of toxic mercury. The level of mercury in the six-hour urine is influenced by the total body burden of mercury, and by the body's ability to detoxify mercury with the chelating agent. Some of these influencing factors may be mineral status of elements such as copper, zinc, selenium and magnesium. Vitamin cofactors such as B-6 are also required for detoxification. Adequate amino acid precursors to important detoxification factors as glutathione are also needed. Adequate nutritional preparation is essential with adequate minerals, vitamin cofactors and amino acid from such sources as whey protein. This also means improvement, if needed, in digestion, assimilation and absorption of nutrients. If the person was in better nutritional and detoxification status for his second test, you could see a higher yield of mercury with use of the same chelating agent and protocol. The second test with a higher level of mercury would then represent a continued increased body burden of mercury, but with an improved detoxification status and ability.

Magnesium is low in both specimens. As the body is going to conserve any minerals that are low or lacking, you would expect to see less in the urine. This patient needs more magnesium replacement. To get a more accurate assessment of mineral status, an RBC element test would be helpful. Elevated copper levels would be expected, as dithiol-chelating agent like DMPS or DMSA, will also pull out copper. If copper were low in urine after use of the chelating agent, you would suspect copper deficiency. It is also important for the patient to be off all seafood two weeks before test, as a large ingestion of fish containing mercury for example could give you transient rises in urine mercury.

QUESTION

What is the clinical relevance of elevated sIgA reported in a Comprehensive Stool Analysis?

ANSWER by Barbara Berta, M.S., R.D., DDI Research Associate and David Quig, Ph.D., DDI V.P. Scientific Support

When sIgA is elevated in the presence of bacterial, fungal or parasitic pathogens, it is a positive sign that the immune system is working and of the body's identification of these organisms and its defensive response. If no pathogens are identified, but sIgA is elevated, consider food allergies/sensitivities or the presence of other elements that the gut immune system identifies as being foreign, inflammatory or toxic.

QUESTION

What is the value of the Lactulose/Mannitol Test?

ANSWER by Tony Hoffman and Jeff Ingersoll, DDI Technical Account Executives

The Lactulose/Mannitol Test challenges the integrity of the intestinal mucosa. Abnormally increased intestinal permeability, most commonly referred to as 'Leaky Gut', can be an underlying contributing factor for allergies, systemic illness and autoimmune diseases. Early signs may be the development of food sensitivities and intolerances. A positive Lactulose/Mannitol test showing impairment of the selective absorption capacity or of the barrier function of the gut, would give direction in treatment choices and aid in diagnosis. A positive or abnormal test could lead to treatment of underlying causes as: low stomach acid or inadequate digestive enzymes, bacterial overgrowth or imbalances (dysbiosis), pathogenic bacteria, yeast or parasites, over use of NSAIDs and antibiotics, and food sensitivities or allergies. Follow-up Lactulose/Mannitol testing is helpful to assess effectiveness of treatment in correcting intestinal permeability problems and in the reducing of antigen leakage through the GI mucosa.

The Lactulose/Mannitol Test utilizes Lactulose, a large molecular sugar, and Mannitol, a small molecular sugar. Upon consumption of known amounts

and timed urine collection, we analyze for the two sugars. Lactulose being a larger molecule should not pass through to the urine, while Mannitol the smaller of the two should. We can assess for two findings with this challenge. High percent Lactulose indicates Intestinal Permeability, while low recovery of Mannitol indicates Malabsorption.

QUESTION

I have been using oral DMSA provocation testing with a six-hour urine to assess mercury and toxic metal burden, but am concerned that I might not be getting the consistent findings I used to find with IV DMPS use. As I am no longer doing IV DMPS, what about oral DMPS for provocation testing?

ANSWER by David Quig, Ph.D., DDI V.P. Scientific Support

Oral DMPS:

Many physicians are not aware of the availability and utility of oral DMPS. Actually, the IV administration of DMPS was intended for the treatment of acute metal poisoning in which circulating blood levels of metals are high. Acute poisoning is quite different from chronic metal toxicity, in which the majority of toxic metals are tightly sequestered inside the cells—not in circulation. Pharmacokinetic studies of Dimaval (Heyltex Corp.) suggest that about 45-60% of orally administered DMPS is absorbed in human subjects and peak urine concentrations of DMPS occur between 2 and 3 hours after oral administration (when taken on an empty stomach). The vast majority of mobilized metals are excreted in the urine within the first 2-4 hours, thereafter the urinary concentration of metals ($\mu\text{g}/\text{gm}$ creatinine) decrease as a result of dilution. Hence for provocation purposes, we recommend a 6 hour urine collection post oral administration of DMPS.

Provocation Protocol:

Several German authors describe oral provocation with DMPS at a flat dose of 300 mg, regardless of the size of the patient. Given that DMPS appears to be absorbed at about 50%, it seems logical to dose patients at approximately 2X the iv dose or 500 mg. One author has described a provocation protocol of 10 mg/kg body weight. All things considered, it seems that a reasonable provocation protocol would entail oral administration of DMPS at either 300 mg (adult), or 10 mg/kg (up to a total of 500 mg), followed by a complete collection of all urine for 6 hr. It is recommended that multi-mineral and sulfhydryl containing supplements (e.g. NAC, GSH, lipoic acid) be withheld 24 hours prior to and on the day of administration of DMPS to maximize availability of the active reduced thiol (SH-) binding sites on the compound.

Summary:

1. Have patient fast for approximately 8 hours.
2. Empty bladder completely prior to administering DMPS orally at 10 mg/kg (up to 500 mg).
3. Consume 0.5 to 1 liter of fluid.
4. Collect ALL urine for the subsequent 6 hours.
5. If necessary, a light meal (no fish!) may be consumed 3-4 hrs. after administering the DMPS.

A separate protocol for the therapeutic use of oral DMPS for metal detoxification is available. These statements have not been evaluated by the Food and Drug Administration. This test is not intended to diagnose, treat, cure or prevent disease.

CAUTION: This document is provided for informational purposes only. The information provided is based upon scientific literature and feedback from DDI clients. It is not a recommendation for treatment of a specific patient. Treating physicians are responsible for determining proper treatment options based upon factors including, but not limited to laboratory analyses, physical exams, symptoms, patient histories, and most importantly, the physician's own judgment. ■