LAB #: F000000-0000-0
PATIENT: Sample Patient
ID: P0000000000
SEX: Female
DOB: AGE: 42

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Stool Chemistry

DIGESTION /ABSORPTION

	Within	Outside	Reference Range
Elastase	437		> 200 µg/mL
Fat Stain	None		None - Mod
Muscle fibers	None		None - Rare
Vegetable fibers	Rare		None - Few
Carbohydrates	Neg		Neg

Elastase findings can be used for the diagnosis or the exclusion of exocrine pancreatic insufficiency. Correlations between low levels and chronic pancreatitis and cancer have been reported. **Fat Stain:** Microscopic determination of fecal fat using Sudan IV staining is a qualitative procedure utilized to assess fat absorption and to detect steatorrhea. **Muscle fibers** in the stool are an indicator of incomplete digestion. Bloating, flatulence, feelings of "fullness" may be associated with increase in muscle fibers. **Vegetable fibers** in the stool may be indicative of inadequate chewing, or eating "on the run". **Carbohydrates:** The presence of reducing substances in stool specimens can indicate carbohydrate malabsorption.

INFLAMMATION

	Within	Outside	Reference Range
Lactoferrin		20.1	< 7.3 µg/mL
Calprotectin*		75	10 - 50 µg/g
Lysozyme*		1060	<= 600 ng/mL
White Blood Cells	None		None - Rare
Mucus	Neg		Neg

Lactoferrin and **Calprotectin** are reliable markers for differentiating organic inflammation (IBD) from function symptoms (IBS) and for management of IBD. Monitoring levels of fecal lactoferrin and calprotectin can play an essential role in determining the effectiveness of therapy, are good predictors of IBD remission, and can indicate a low risk of relapse. **Lysozyme*** is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. **White Blood Cells** (WBC) and **Mucus** in the stool can occur with bacterial and parasitic infections, with mucosal irritation, and inflammatory bowel diseases such as Crohn's disease or ulcerative colitis.

IMMUNOLOGY

	Within	Outside	Reference Range
Secretory IgA*		358	51 - 204 mg/dL

Secretory IgA* (sIgA) is secreted by mucosal tissue and represents the first line of defense of the GI mucosa and is central to the normal function of the GI tract as an immune barrier. Elevated levels of sIgA have been associated with an upregulated immune response.

Comments:

Date Collected: 01/25/2015
Date Received: 01/30/2015
Date Completed: 02/06/2015

*For Research Use Only. Not for use in diagnostic procedures.
Methodology: Elisa, Microscopy, Colormetric, Gas Chromotography, ph Electrode

LAB #: F000000-0000-0
PATIENT: Sample Patient
ID: P0000000000
SEX: Female
DOB: AGE: 42

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174 U.S.A.

Stool Chemistry

SHORT CHAIN FATTY ACIDS

	Within	Outside	Reference Range
% Acetate	48		40 - 75 %
% Propionate	25		9 - 29 %
% Butyrate	24		9 - 37 %
% Valerate	2.7		0.5 - 7 %
Butyrate	2.5		0.8 - 4.8 mg/mL
Total SCFA's	10		4 - 18 mg/mL

Short chain fatty acids (SCFAs): SCFAs are the end product of the bacterial fermentation process of dietary fiber by beneficial flora in the gut and play an important role in the health of the GI as well as protecting against intestinal dysbiosis. Lactobacilli and bifidobacteria produce large amounts of short chain fatty acids, which decrease the pH of the intestines and therefore make the environment unsuitable for pathogens, including bacteria and yeast. Studies have shown that SCFAs have numerous implications in maintaining gut physiology. SCFAs decrease inflammation, stimulate healing, and contribute to normal cell metabolism and differentiation. Levels of **Butyrate** and **Total SCFA** in mg/mL are important for assessing overall SCFA production, and are reflective of beneficial flora levels and/or adequate fiber intake.

INTESTINAL HEALTH MARKERS

	Within	Outside	Reference Range
Red Blood Cells	None		None - Rare
pH	6.6		6 - 7.8
Occult Blood	Neg		Neg

Red Blood Cells (RBC) in the stool may be associated with a parasitic or bacterial infection, or an inflammatory bowel condition such as ulcerative colitis. Colorectal cancer, anal fistulas, and hemorrhoids should also be ruled out.
pH: Fecal pH is largely dependent on the fermentation of fiber by the beneficial flora of the gut.
Occult blood: A positive occult blood indicates the presence of free hemoglobin found in the stool, which is released when red blood cells are lysed.

MACROSCOPIC APPEARANCE

	Appearance	Expected
Color	Brown	Brown
Consistency	Loose/Watery	Formed/Soft

Color: Stool is normally brown because of pigments formed by bacteria acting on bile introduced into the digestive system from the liver. While certain conditions can cause changes in stool color, many changes are harmless and are caused by pigments in foods or dietary supplements. **Consistency:** Stool normally contains about 75% water and ideally should be formed and soft. Stool consistency can vary based upon transit time and water absorption.

INTRODUCTION

This analysis of the stool specimen provides fundamental information about the overall gastrointestinal health of the patient. When abnormal microflora or significant aberrations in intestinal health markers are detected, specific interpretive paragraphs are presented. If no significant abnormalities are found, interpretive paragraphs are not presented.

Lysozyme

The level of lysozyme, a biomarker of inflammation, is elevated in this specimen. Lysozyme is an enzyme that catalyzes the hydrolysis of specific glycosidic bonds in mucopolysaccharides that constitute the cell wall of gram-positive bacteria. Lysozyme is an antibacterial defense present in the G.I. tract and is secreted by granulocytes, macrophages, Paneth cells, and Brunner's Glands as well as normal colonic crypt cells [1]. The main source for fecal lysozyme is the intestinal granulocytes.

Moderate elevations in fecal lysozyme are commonly associated with significant overgrowth of enteropathogens such as yeast or dysbiotic bacteria. Markedly elevated levels of fecal lysozyme have been identified in colonic inflammatory bowel disease (IBD), such as Crohn's disease and ulcerative colitis as well as other non-IBD G.I. diseases with diarrhea, compared to healthy controls [2,3]. In Crohn's disease, excess lysozyme may be a result of active secretions of macrophages in the lamina propria, and monocytic cells in the granulomas (sites of G.I. inflammation) [4]. In ulcerative colitis, it has been postulated that elevations in fecal lysozyme may be secondary to intestinal loss of granulocytes and their secretory granules [5]. Additionally, Paneth cell metaplasia, a phenomenon that occurs with various inflammatory conditions of the large intestine, may be a minor contributor to fecal lysozyme elevations [5]. Paneth cells are part of the intestinal epithelial lining found in the deepest part of intestinal cryptwhich are the crypts of Lieberk□hn. Paneth cells contain lysozyme in their secretory granules, and combined with their phagocytic capability, help to regulate intestinal microbial flora [5].

Lysozyme is helpful in the determination of colonic inflammatory activity rather than small bowel disease [2]. Slightly elevated levels of lysozyme may be treated with anti-inflammatory agents or by removing the antagonist, such as enteroinvasive microorganisms or allergens. Moderate to high levels of lysozyme (>2,000) may indicate an active inflammatory bowel condition which often requires further testing such as colonoscopy. To rule out IBD, check fecal lactoferrin levels (elevated with IBD).

1. Saito H, Ksajima T, Masuda A, et al. Lysozyme localization in human gastric and duodenal epitheleum. Cell Tissue Res 1988; 251:3-7-313.
2. Van der Sluys Veer A, Brouwer J, Biemond I, et al. Fecal lysozyme in assessment of disease activity in inflammatory bowel disease. Dig Dis & Sci. 1998;43(3):590-5.
3. Klass HJ, Neale G. Serum and faecal lysozyme in inflammatory bowel disease. Gut 1978;19:233-9.
4. Geboes K, Van den Oord JJ, Rutgeerts P, et al. Immunohistochemical identification of lysozyme in pseudopyloric gland metaplasia in Crohn's disease. Hepatogastroenterology 1986;90:1121-8.
5. Stamp GWH, Poulsom R, Chung LP, et al. Lysozyme gene expression I inflammatory bowel disease. Gastroenterol 1992;103:532-538.

Fecal Lactoferrin

The level of fecal lactoferrin, a biomarker of serious gastrointestinal inflammation, is abnormally high in this fecal sample. Fecal lactoferrin is elevated in association with Inflammatory Bowel Disease (IBD) such as Ulcerative Colitis (UC) or Crohn's Disease (CD)[1,2], but NOT Irritable Bowel Syndrome (IBS)[1,3]. Therefore, assessment of fecal lactoferrin levels enables distinction between IBD and non-inflammatory IBS. Such distinction is critical because, although both IBD and IBS may share some common symptoms such as diarrhea, abdominal cramping and weight loss, the diseases are treated quite differently. IBD may become life threatening, requires life long treatment and possibly surgery. In contrast, IBS is often effectively treated with dietary restrictions, stress reduction and medication.

Gastrointestinal inflammation associated with IBD is associated with increased infiltration of activated neutrophils into the mucosa and increased release of lactoferrin into the gut[1,4,5]. Patients with inflammation of the GI tract, such as IBD (but not IBS), exhibit elevated lactoferrin concentrations in the feces[1].

Clinical studies have shown that fecal lactoferrin levels of healthy persons are similar to IBS patients, but markedly increased in patients with active IBD[1,3]. Patients with IBD oscillate between active and inactive disease states, and fecal lactoferrin levels increase 2-3 weeks prior to onset of clinical symptoms[6]. During remission and effective treatment, fecal lactoferrin decreases significantly. Therefore disease activity, and efficacy of treatment can be monitored by following fecal lactoferrin levels. The test can be ordered separately to track disease activity in patients with IBD.

Moderately elevated levels of fecal lactoferrin can occur, with fecal red blood cells and leukcytes, in association with invasive enterpathogens [7,8]. Such levels would be expected to be much lower than those associated with the active phase of IBD. Therefore, with moderately elevated levels of fecal lactoferrin, one should check for the presence of enteropathogens (eg. Shigella, Campylobacter, Clostridium difficile).

Guidelines for interpreting the results of this test are provided by the results of a large multi-center clinical study which evaluated fecal lactoferrin levels in 180 patients suffering with IBS and IBD (UC and CD) compared to 56 healthy controls.

		FECAL LACTOFERRIN	
GROUP	# of SPECIMENS	mean mcg/ml	SE
Inactive UC	41	67	24
Active UC	31	815	789
Inactive CD	26	239	83
Active CD	51	672	242
IBS	31	1.3	0.3
Healthy Controls	55	1.6	0.4

1. Kane, S.V., Sandborn, W.J., Rufo, P.A., et al. Am. J. Gastroenterol. (2003)98(6):1309-14.

Secretory IgA (sIgA)

The concentration of sIgA is abnormally high in this fecal specimen. Immunological activity in the gastrointestinal tract can be assessed using secretory immunoglobulin A (sIgA). Secretory IgA is the predominant antibody or immune protein the body manufactures and releases in external secretions such as saliva, tears, and milk [1]. It is also transported through the epithelial cells that line the intestines out into the lumen. Secretory IgA represents the first line of defense of the GI mucosa and is central to the normal function of the GI tract as an immune barrier [1]. As the principal immunoglobulin isotype present in mucosal secretions, sIgA plays an important role in controlling intestinal milieu which is constantly presented with potentially harmful antigens such as pathogenic bacteria, parasites, yeast, viruses, abnormal cell antigens, and allergenic proteins [1]. Secretory IgA antibodies exert their function by binding to antigenic epitopes on the invading microorganism limiting their mobility and adhesion to the epithelium of the mucus membrane [2]. This prevents the antigens from reaching systemic circulation allowing them to be excreted directly in the feces. Elevated fecal sIgA is an appropriate response to an antigenic presence. Microbial and microscopic studies of the stool are useful in identifying if bacteria, yeast, or parasites are present. Eradication of the pathogenic microorganisms will bring sIgA back down into the normal range. Elevated sIgA levels have been observed in the absence of bacteria, yeast or parasites, in individuals with atopic conditions such as food allergies, urticaria, and dermatitis.

References:

1 Crago SS, Tomasi TB. Mucosal Antibodies, Food Allergy and Intolerance. Bailliere Tindall/W.B. Saunders 1987;167-89.
2 Roberts JA. Factors predisposing to urinary tract infections in children. Ped Neph 1996;10:517-522.
3 Carins J, Booth C. Salivary immunoglobulin-A as a marker of stress during strenuous physical training. Aviat Space Environ Med 2002;73(12)1203-7.
4 Teodosio MR, Oliveira ECM. Urinary secretory IgA after nutritional rehabilitation. Braz J Med Biolog Res 1999;32-421-426
5 Alverdy J. Effects of glutamine-supplemented diets on immunology of the gut. J Parent Enteral Nutr 1990;14(4):1095-1135.
6 Burke DJ, et al. Glutamine-supplemented total parenternal nutrition improves gut function. Arch Surg 1989;24:2396-2399.
7 Alverdy JA. The effect of total parenternal nutrition on gut lamina propria cells. J Parent. Enteral Nutr 1990;14(suppl).
1 Qamar A, Aboudola S, Warny M, et al. Saccharomyces boulardii stimulates intestinal immunoglobulin A immune response to clostridium difficile toxin A in mice. Infect Immun 2001;69(4):2762-5.
2 Buts JP, Bernasconi P, Vaerman JP, et al. Stimulation of secretory IgA and secretory component of immunoglobulins in small intestine of rats treated with Saccharomyces boulardii. Dig Dis Sci 1990;35(2):251-6.

Fecal Calprotectin

The level of fecal Calprotectin is higher than expected. Elevated fecal Calprotectin and Lactoferrin levels indicate the presence of neutrophils and inflammation in the gastrointestinal (GI) mucosa. Calprotectin and Lactoferrin facilitate differentiation between irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). IBD includes autoimmune conditions such as Crohns disease and ulcerative colitis (UC); these conditions may become life-threatening and require lifelong treatment.

For patients 4 years old to adults (Manz 2012; Fagerberg 2005):

High levels of Calprotectin (> 200 µg/gm) are associated with active IBD and gastrointestinal

inflammation; elevation may also occur due to bacterial infection, colitis or sometimes, cancer. Fecal Calprotectin should be reassessed after about 4 weeks for confirmation.

Moderate calprotectin (50-200 µg/gm) is an indicator of chronic inflammation. Inflammation at this level may be due to IBD in remission or inflammation caused by non-steroidal anti-inflammatories (NSAIDs). Levels should be reassessed after about 4 weeks. Low levels of Calprotectin (< 50 µg/gm) are usually associated with viral GI infections or non-inflammatory bowel conditions such as IBS.

Multiple studies have shown fecal Calprotectin and Lactoferrin to be equivalent with respect to clinical sensitivity and specificity. Studies suggest that Calprotectin may correlate more closely with histological (cell microscopy) findings. Lactoferrin may correlate better to macroscopic (endoscopy) findings, and may be the better indicator of impending relapse, elevating 2-3 weeks prior to clinical symptoms.

Chronic inflammation of the gastrointestinal mucosa contributes to symptoms of IBD. Chronic stress is known to contribute to symptom flare-ups and increased inflammation. Liver disease or the use of aspirin or nonsteroidal anti-inflammatory (NSAID) medications may elevate Calprotectin levels. Fecal Calprotectin levels may also be increased in newborns.

References:

Carroccio, Antonio; Iacono, Giuseppe; Cottone, Mario; Di Prima, Lidia; Cartabellotta, Fabio et al. (2003)
Diagnostic Accuracy of Fecal Calprotectin Assay in Distinguishing Organic Causes of Chronic Diarrhea from Irritable Bowel Syndrome: A Prospective Study in Adults and Children
Clin. Chem. vol. 49 (6) p. 861-867

Fagerberg, Ulrika Lorentzon; Lööf, Lars; Myrdal, Urban; Hansson, Lars-Olof; Finkel, Yigael
Colorectal Inflammation is Well Predicted by Fecal Calprotectin in Children with Gastrointestinal Symptoms
Journal of Pediatric Gastroenterology & Nutrition: April 2005 - Volume 40 - Issue 4 - pp 450-455

Lamb, C.A.; Mansfield, J.C. (2011)
Measurement of faecal calprotectin and lactoferrin in inflammatory bowel disease.
Frontline gastroenterology vol. 2 (1) p. 13 - 18

Manz, Michael; Burri, Emanuel; Rothen, Claude; Tchanguizi, Nuschin; Niederberger, Christian et al. (2012) Value of fecal calprotectin in the evaluation of patients with abdominal discomfort: an observational
study. BMC gastroenterology vol. 12 p. 5

Said, Hesham Ezz El Din, et al. (2013)
The diagnostic value of faecal calprotectin in differentiating inflammatory bowel diseases (IBD) from irritable bowel syndrome (IBS)
Report and Opinion, 2011;3(1)

Vieira, Andrea; Fang, Chia; Rolim, Ernani; Klug, Wilmar; Steinwurz, Flavio et al. (2009)
Inflammatory bowel disease activity assessed by fecal calprotectin and lactoferrin: correlation with laboratory parameters, clinical, endoscopic and histological indexes
BMC Research Notes vol. 2 (1) p. 221