

**Gut-Well™** **Accession: 555555**

**Healthcare Professional**

Dr. Feel Good  
100 Healthy Street  
Calgary, AB T3B 1J5

**Patient**

Jacob Smith  
123 - 4th Ave NW  
Calgary, AB T1G 3M3  
P:403-555-1234

Age: 32  
Date of Birth: 1985/02/07  
Gender: Male

P: 403-555-2345  
F:



Stool Colour  
Consistency

Brown  
Liquid

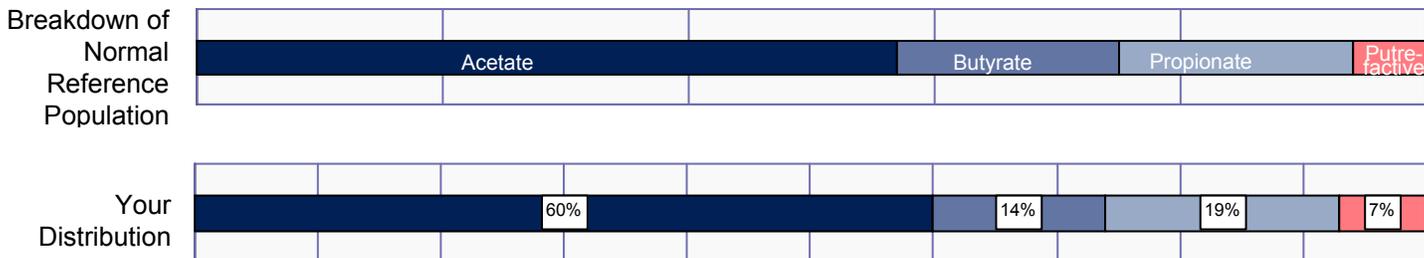
*Short Chain Fatty Acid (SCFA) Profile*

| Analyte  | Result | Range     | 0% | 20% | 40% | 60% | 80% | 100% | Rank |
|--|--------|-----------|----|-----|-----|-----|-----|------|------|
| Total SCFA (umol/mL)   | 58     | 70 - 180  |    |     |     |     |     |      | 11%  |
| Total Beneficial SCFA (umol/mL)<br><i>Fiber/Carbohydrate-derived</i> | 54     | 63 - 180  |    |     |     |     |     |      | 11%  |
| Total Putrefactive SCFA (umol/mL)<br><i>Protein-derived SCFA</i>     | 4.1    | 3.8 - 9.7 |    |     |     |     |     |      | 19%  |
| n-Butyrate (umol/mL)   | 8.3    | 9.4 - 43  |    |     |     |     |     |      | 14%  |

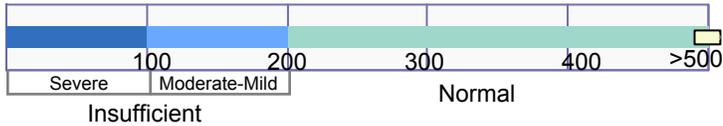
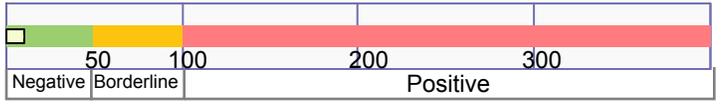
*SCFA Distribution (percentages of Total SCFA)*

Normal Distribution:

- Acetate (52 - 62%)
- Propionate (15 - 22%)
- Butyrate (12 - 24%)
- Putrefactive (3 - 8%)



Other Stool Chemistry

| Fecal Analytes        | Result | Range       |  | Rank |
|-----------------------|--------|-------------|--|------|
| Extractable fat (%)   | 3.4    | 2.8 - 6.4   |  | 26%  |
| Elastase (ug/mL)      | 610    | >200        |  | n/a  |
| Calprotectin (ug/mL)  | < 5.0  | <100        |  | n/a  |
| Secretory IgA (ug/mL) | 1,300  | 930 - 6,500 |  | 21%  |

Note:  $\mu\text{g/mL} \approx \mu\text{g/g}$  fresh stool

Microbiology

Stool Culture

|               |          |   |
|---------------|----------|---|
| Report Status |          | - 10 day cold enrichment for Yersinia i performed on all stool specimens. Further report will follow if positive.   |
| Organism 1    | Abnormal | Final<br><b>SALMONELLA SPECIES</b><br>- Salmonella gastroenteritis is usually a self-limited illness not requiring antibiotic treatment unless symptoms are severe or patient is immunocompromised, < 6 months old or > 50 years old.<br>- Referred to BCCDC for speciation<br>- Result sent to Public Heal |
| Organism 2    |          | SALMONELLA SPECIES (previously reported) serotyped by BCCDC as  |
| Organism 3    | Abnormal | <b>AEROMONAS HYDROPHILA GROUP</b><br>- Result sent to Public Heal   |
| Organism 4    | Abnormal | <b>Salmonella enteritidis.</b><br><b>CAMPYLOBACTER JEJUNI</b><br>- Result sent to Public Heal   |

Antibiotic Susceptibility

|                    | Org1 | Org3 | Org4 |
|--------------------|------|------|------|
| AMPICILLIN         | S    |      |      |
| TRIMETHOPRIM-SULFA | S    | S    |      |
| CEFTRIAZONE        | S    | S    |      |
| CEFIXIME           | S    |      |      |
| TETRACYCLINE       |      | S    |      |
| ERYTHROMYCIN       |      |      | S    |
| AZITHROMYCIN       |      |      | S    |

**Clostridium difficile Toxin Assay**

Result Status  
Clostridium difficile Toxin (PCR/NAAT)  
Stool

Final  
Negative for Toxigenic Clostridium difficile by  
nucleic acid amplification.

*Parasitology*

**Ova and Parasite Examination**

Report Status  
Result

**Abnormal**

- Specimen #1  
Final  
**GIARDIA LAMBLIA CYSTS**  
- Result sent to Public Health

**Ova and Parasite Examination**

Report Status  
Result

**Abnormal**

- Specimen #2  
Final  
**BLASTOCYSTIS HOMINIS**

**Ova and Parasite Examination**

Report Status  
Result

**Abnormal**

- Specimen #3  
Final  
**OOCYSTS OF CYCLOSPORA SPECIES**  
- Result sent to Public Health



Note: The College of Physicians and Surgeons of Alberta - To be determined

George Gillson MD, PhD  
Medical Director

### SHORT-CHAIN FATTY ACIDS OVERVIEW

Historically, humans ate large amounts of plants: fruits, vegetables, seeds, nuts. These all contain a vast array of complex molecules loosely referred to as fibre. Researchers have studied and categorized this plant-derived material endlessly: insoluble fibre, soluble fibre, non-starch fibre, simple sugars, starch, resistant starch, pectin and so on. In this report, for simplicity we will refer to the entire collection as "fibre/carbohydrate."

The short-chain fatty acids measured in this test consist of straight-chain and branched-chain varieties. The straight-chain fatty acids come from the catabolism or "fermentation" of fibre/carbohydrate substrates and they are commonly referred to as "Beneficial" fatty acids. (Valerate is a straight chain fatty acid that can arise from both plant and animal sources, but most commonly it is included in the tally of Putrefactive fatty acids. It normally comprises approximately 2% of the total fatty acids in stool.) The branched-chain fatty acids arise primarily from the catabolism of animal proteins from flesh and eggs. The branched-chain fatty acids are referred to as "Putrefactive" fatty acids.

Both classes of fatty acids are critical to survival, growth and repair, despite the somewhat archaic class names.

Wong, J., et al. Colonic Health: fermentation and short chain fatty acids. *J Clin. Gastroenterol.* 2006. 40(3):235-243  
Tan, J., et al. The role of short-chain fatty acids in health and disease. *Advances in Immunology.* Chapter 3. 2014. Vol 121: 91-119.

Rios-Covian, D., et al. Intestinal Short Chain Fatty Acids and their link with Diet and Human Health. *Frontiers in Microbiology.* 2016. 7(185):1-9.

### TOTAL SCFA IN BOTTOM TERTILE

The principal short-chain fatty acids consist of the beneficial (fibre/carbohydrate-derived) fatty acids acetate, propionate and butyrate, and the putrefactive (protein-derived) fatty acids valerate, iso-valerate and iso-butyrate. Valerate is a special case. (see overview.)

In general, a normal level of total short-chain fatty acids reflect overall health of the colonic bacterial population. This in turn reflects intake of fibre/carbohydrate-containing foods and also reflects the nature of the bacterial community (species diversity, presence/absence of keystone organism).

This patient's result for total short-chain fatty acids is in the lower third of the reference distribution. Low total SCFAs may be seen in inflammatory bowel disease, irritable bowel syndrome, colorectal cancer, low fibre/carbohydrate-containing food intake and antibiotic use (especially IV, multiple antibiotics sequentially or concurrently, chronic antibiotic use/multiple courses per year).

Low total SCFA results can also be seen in calorie-restricted diets, starvation and fasting as well as long intestinal transit time. Long transit time allows for more absorption of short-chain fatty acids into the systemic circulation, leaving fewer fatty acids arriving at the distal colon.

### TOTAL BENEFICIAL (FIBRE/CARBOHYDRATE-DERIVED) SCFA IN BOTTOM TERTILE

The beneficial fatty acids consist of acetate, propionate and n-butyrate. Of the three main fatty acids listed above, acetate typically makes up approximately half of the total. Valerate is also considered by some to be a beneficial short-chain fatty acid although it correlates more strongly to the putrefactive fatty acids in our reference population.

This patient's result for total fibre/carbohydrate-derived short-chain fatty acids is in the lower third (bottom tertile) of the reference distribution. The comments for this finding are basically the same as those for total short-chain fatty acids, since the beneficial fatty acids typically comprise 90-95% of all short-chain fatty acids. As discussed above, beneficial fatty acids arise from consumption of fibre/carbohydrate-containing foods.

Wong, J., et al. Colonic Health: fermentation and short chain fatty acids. *J Clin. Gastroenterol.* 2006. 40(3):235-243  
Shi, Y., et al. Function and clinical implications of short-chain fatty acids in patients with mixed refractory constipation. *Colorectal Disease.* 2016. 18:803-810.

**TOTAL PUTREFACTIVE (PROTEIN-DERIVED) SCFA IN LOWEST TERTILE**

The principal putrefactive (protein-derived) short-chain fatty acids are valeric, isovaleric and isobutyric acid. In aggregate they comprise about 5% of the total short-chain fatty acids.

For this patient, total putrefactive fatty acids are in the lowest third (bottom tertile) of the reference distribution.

In adults, this is generally taken to reflect low protein intake which could be seen in frequent fasting. Individuals following Vegetarian or Vegan diets may exhibit low putrefactive short-chain fatty acids.

The number of young children (< 3 years old) in our reference population was small compared to the adult population. The finding of low putrefactive fatty acids should be interpreted in light of the clinical situation (dietary history, overall health) in children under the age of three years.

**n-BUTYRATE IN BOTTOM TERTILE**

n-Butyrate is a 4-carbon fatty acid produced in the large intestine by numerous species of bacteria as a metabolic end-product of dietary fiber and carbohydrate fermentation. Once synthesized and secreted by the microflora, butyrate is rapidly absorbed by colonocytes where it serves numerous functions related to colonic cell metabolism and homeostasis. As the major energy substrate for colonic epithelial cells, butyrate supports cellular proliferation, survival and maintenance of a normal colonocyte phenotype. In a paradoxical fashion, butyrate has anti-carcinogenic properties in the colon, by acting as a HDAC inhibitor and promoting apoptosis in cancerous cells. Butyrate acts as a potent anti-inflammatory agent in the colon by inhibiting the master pro-inflammatory NF- $\kappa$ B pathway, and can increase intestinal barrier integrity by up-regulating the expression of mucin glycoproteins. As a result of the numerous beneficial functions of butyrate, it has come to be considered a biomarker of overall colonic health. Since it is rapidly absorbed and metabolized by colonocytes, concentrations of butyrate are negligible in the blood and so fecal samples are used to assess production.

The n-butyrate result for this patient lies in the bottom third (bottom tertile) of the reference distribution. Low butyrate is associated with colorectal cancer, inflammatory bowel disease, irritable bowel syndrome. The most probable cause of low n-butyrate is insufficient intake of foods high in resistant starches, such as: lentils, chickpeas, buckwheat, kidney beans, millet, brown rice, garlic, asparagus, leeks, onions, green bananas, Jerusalem artichoke.

Long transit times may lead to low fecal butyrate as more time is afforded for butyrate to be absorbed into the systemic circulation before it can reach the distal colon. Absence of butyrogenic flora due to antibiotic use and disrupted ecology due to pathogen overgrowth should also be considered when n-butyrate is low.

Tan, J., et al. The Role of Short Chain Fatty Acids in Health and Disease. *Advances in Immunology*. 2014. 121:91-119.

Pryde, S., et al. The microbiology of butyrate formation in the human colon. *FEMS Microbiology Letters*. 2002. 217:133-139.

Rios-Covian, D., et al. Intestinal Short Chain Fatty Acids and their link with Diet and Human Health. *Frontiers in Microbiology*. 2016. 7(185):1-9.

Sivaprakasam, S., et al. Benefits of short-chain fatty acids and their receptors in inflammation and carcinogenesis. *Pharmacology & Therapeutics*. 2016. 164:144-151.

Zateski, A., et al. Butyric acid in irritable bowel syndrome. *Prz Gastroenterology*. 2013. 8(6):350-353.

**PROPORTIONS OF ACETATE, BUTYRATE, PROPIONATE AND PUTREFACTIVE SCFA WITHIN NORMAL RANGE: TOTAL SCFAs LOW**

The proportions of acetate, butyrate, propionate and putrefactive short-chain fatty acids relative to the total short-chain fatty acids are within normal limits for this patient despite overall low total short-chain fatty acids.

**FECAL FAT PERCENTAGE IN LOWEST TERTILE**

The percentage of solvent-extractable fats is within the bottom or lowest third (lowest tertile) of the reference distribution. This patient is most likely eating a diet low in fats compared to our reference population. Low fat intake may be associated with dry skin, eczema, dry hair and low levels of fat-soluble vitamins (A,E,D,K).

**ELASTASE ABOVE 500 ug/mL**

Elastase below 200 ug/mL is considered low. Although this patient's result for elastase lies above 500 ug/mL, results in this range are not an abnormal finding in the population tested to establish our reference ranges.

**CALPROTECTIN NEGATIVE**

Calprotectin is derived from neutrophils drawn to the site of active inflammation in the colonic mucosa. Elevated calprotectin is correlated to the presence and severity of inflammatory bowel disease and is also elevated in the setting of diverticulitis, malignancy and infection. Normal or negative calprotectin helps to distinguish between inflammatory bowel disease and irritable bowel syndrome.

The cutoff for normal or negative Calprotectin is 50 ug/mL. This patient's result is negative or normal.

**SECRETORY IgA IN LOWEST TERTILE**

Secretory IgA (sIgA) is the principle antibody present in colonic epithelial secretions. It plays a central role in continuous fine-tuning of the balance between normal flora, and in detection of pathogens. Other key roles include maintenance of GI barrier function and maintenance of a healthy microbial population.

The sIgA result is in the lowest third (lowest tertile) of the reference distribution. Low sIgA levels can be seen in association with chronic stress, malnutrition/dietary restriction, congenital deficiency, excessive alcohol intake, chronic nonsteroidal anti-inflammatory use, use of glucocorticoids and antibiotics.

Serum total IgA testing may be indicated if a congenital abnormality is suspected.

Low sIgA is not diagnostic of any clinical condition. Repeat testing may be helpful in the assessment of various interventions such as dietary modification, and pre-/probiotic therapies.

Henderson, P., et al. Function of the intestinal epithelium and its dysregulation in inflammatory bowel disease. *Inflamm Bowel Dis*. 2011. 17:382-395.