Dear friend,

I am very pleased to share with you the Spring 2013 edition of Network, a publication of the Familial Gastrointestinal Cancer Registry.

At the Zane Cohen Centre for Digestive Diseases, we are fortunate to have an outstanding team of over 40 national and international researchers and clinicians, whose varied work is reflected in this edition. We have featured some of our newer team members in the Meet and Greet section.

I do hope you find the research findings informative, and the patient support material instructive. We look forward to both your feedback and support for our work — for you and for the generations to come.

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Education Night for Lynch Syndrome Families coming up on June 11, 2013

Lynch syndrome is a rare genetic condition that greatly increases the risk to develop cancer, primarily colorectal and endometrial cancer. At one time, it was thought that all colorectal cancer followed a similar pathway to becoming cancerous, but we now know that this is not the case. While most lectures on colorectal cancer refer to the general population, talks for families with Lynch syndrome should be tailored to the research on risk, screening, and treatment of cancers in these families.

It was for that reason that an education night just for patients with Lynch syndrome was created. We began hosting this night in 2003 and over the years, have invited surgeons, gastroenterologists, gynecologists, pathologists, family physicians, dermatologists and psychologists to update our families on the latest research and understanding of this syndrome. We also invited patients with Lynch syndrome to share their stories, which were always greatly appreciated by the audience.

We will be hosting the 5th biennial Education Night on June 11, 2013. If your family has Lynch syndrome, you should find a special flyer in this mailing with details on the speakers for this night, along with the time. If you have not received a flyer and are interested in attending, please feel free to contact us at 416-586-4800 ext. 5112 and we can add you to the mailing list designed for this evening.
RESEARCH UPDATE

The Effect of Aspirin on Colorectal Cancer in Lynch Syndrome
Kara Semotiuk, MS (C)CGC, Genetic Counsellor

CAPP2 was a randomized controlled trial that looked at the effects of aspirin and resistant starch on colorectal cancer risk for individuals with the hereditary cancer condition called Lynch syndrome (LS), also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC).

It is well known that individuals with LS have a significantly increased risk for colorectal cancer and other cancers, compared to the general population. In this study, the aim was to determine whether taking aspirin or starch for an extended period of time would affect the incidence of colorectal cancer in this population.

Study participants were randomly and blindly assigned to one of four groups: taking aspirin, aspirin placebo, starch, or starch placebo for up to 4 years. Participants were followed during the study phase and some were also followed after the trial was complete. Analysis showed that for those taking aspirin, the colorectal cancer risk was about half that of the placebo group only after 7 years of follow-up.

From this, it seems that taking aspirin in some cases showed a delayed rather than an immediate protection against colorectal cancer. It is important to note that the amount of aspirin given was quite high, at 600 mg/day. The next phase of the study, called CAPP3, will begin soon, where the aim will be to establish the optimum dose and duration of aspirin to recommend for people with LS. Please speak to your family doctor before taking aspirin, as it has other purposes and side effects. And for those with LS, stay tuned for CAPP3 recruitment information!

A New Research Study with the Terry Fox Research Institute
Spring Holter, MS (C)CGC, Genetic Counsellor

On October 1, 2012, the Terry Fox Research Institute began funding a 5-year study to look at known genetic factors that cause colorectal cancer (CRC); to see how family members get screened for CRC; and to look for new genes that may give some families a higher chance of developing CRC. This study includes sites in five Canadian provinces and is being led by Dr. Steven Gallinger at Mount Sinai Hospital.

Individuals with a family history of CRC are at increased risk for this disease. Having a first-degree relative (parent, child, or sibling) with CRC approximately doubles the risk, which increases further with the number of relatives affected, particularly if they are diagnosed at younger ages (usually <50 years). Lynch Syndrome (LS), also known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), is the most common form of hereditary CRC and is caused by mutations in one of 5 different genes. Screening for LS in CRC patients can be done relatively easily through a tumour test performed on a patient’s CRC surgical specimen.

Despite recent advances in our understanding of genetic predisposition to CRC, a large fraction of high-
We Build Knowledge To Improve Treatment

risk Canadian LS families are not being identified and are, therefore, unknowingly missing an important opportunity for CRC prevention, early detection, and potential novel therapeutics.

This new study will be drawing on the expertise of the surgical, pathology, and genetics departments at Mount Sinai Hospital as routine screening for LS has been performed at Mount Sinai Hospital since the summer of 2010. We were the first in Canada to begin routine screening for LS on all CRC patients diagnosed under the age of 60 who had surgery at Mount Sinai Hospital. To date, 83 individuals have had LS tumour screening and, of those, 9 patients (11%) have been found to have LS.

We will also be looking at how relatives follow colonoscopy recommendations and the factors that influence whether or not they participate in CRC screening. In addition, families with a strong history of CRC will be asked to provide DNA samples so that we may try to find new genes that cause CRC.

In 2012, our centre joined forces with the Hospital for Sick Children to form an international consortium for children who have inherited Lynch syndrome from both of their parents. This rare condition is known as biallelic mismatch repair syndrome, which refers to having two mutated copies of the mismatch repair genes that cause Lynch syndrome. Having two parents with Lynch syndrome is a rare occurrence; however, it is more common in some parts of the world where distant relatives marry.

Children who inherit Lynch syndrome from both of their parents are at high risk to develop cancer in childhood, such as brain and blood cancers. The goal of the consortium is to better understand the cancer risk that impacts these families and determine the best way to screen and prevent these cancers from occurring.

In 2011, our team published cancer screening guidelines to help detect cancer at a treatable stage in these children. These guidelines are now being used worldwide to follow-up on families with biallelic mismatch repair syndrome. To date, we have 15 families from 8 countries that have this rare condition and they are working with us to improve our understanding of the condition and help diagnose and treat these rare cancers.

For more information, please contact us:
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**Polyps of the Small Intestine in FAP Patients**

*Pablo E. Serrano, MD, MPH, MSBS, HPB Fellow*

We know that patients with FAP have a gene mutation that predisposes them to multiple precancerous polyps called **adenomas** in the large bowel, or **colon**. More than 30 years ago, we also learned that adenomas can develop in the small intestine, clustering in a particular area beyond the stomach called the **duodenum** where bile and pancreatic juices enter the bowel. Whereas improvements in the screening and early resection of the large bowel have markedly improved the lives of patients, one of the most common tumours in FAP remains cancer of the small bowel.

As opposed to colonic polyps, not everyone with FAP will develop polyps in the small bowel; however, as patients get older, there is a higher risk of developing them. In addition, small bowel polyps tend to grow more slowly than colonic polyps. Compared to surgical resection of the colon, surgical resection of the duodenum carries a higher risk of complications, therefore, **duodenectomy** or **pancreaticoduodenectomy** (Whipple procedure) is not our first choice for prevention of small bowel cancer in FAP.

In order to prevent deaths from duodenal cancer, our team at the Familial GI Cancer Registry developed a protocol in 1990 to prevent these polyps from progressing to cancer, with the additional objective of avoiding unnecessary surgery.

The protocol includes having regular check-ups with upper endoscopies or **esophagogastroduodenoscopy** (EGD) with a side-viewing endoscope to look at the areas of the small bowel where these polyps may develop. Based on the results of the upper endoscopy, patients are classified into four different groups or stages.

Follow-up and management depends on the stage of disease of the small intestine. Since 1982, we have followed a total of 287 patients with this regular check-up protocol. We found that the majority of patients with FAP (65%) will have small 1-2 mm polyps in the small intestine.

Most patients in this group did not progress with worsening polyps and they rarely developed cancer. The occasional patient will have medium or large polyps that will require closer attention because they are of more concern. We followed 98 patients in this latter category over 30 years and found that there was a 42% risk of progression from medium-sized polyps to larger-sized polyps (lesions 10 mm or greater) over 5 years. Once the size of the polyps reached 10 mm or greater, we recommend their removal because we now know they have a higher likelihood of having worrisome changes – something we call **high-grade dysplasia** – and a higher chance of changing to cancer.

The removal of larger-sized polyps can be accomplished through endoscopic techniques by completely excising the polyp using snares or endoscopic knives. If the polyp is too big for endoscopic removal, we offer surgical resection of the area where the polyps are clustered. In our study, 50% of patients underwent endoscopic procedures to remove polyps and 20% needed surgical resection, including 16 Whipple procedures.

Recurrence of polyps is high, but with our approach, only 5 patients (1.7% of all patients followed) developed cancer of the small bowel. The risk of large polyps changing to cancer was only 2% over 10 years. Our management strategy is intended to prevent the development of cancer of the small bowel in FAP.
Unfortunately, cancer can develop at a very young age in FAP (average 58 years old) and approximately 2% of patients die from duodenal cancer, since some patients have other health issues (like heart disease, desmoids, pancreatitis or other cancers) that hinder them from having regular follow-up. Nevertheless, our surveillance and treatment protocol was very effective in preventing deaths from duodenal cancer in patients who were able to comply with the approaches described above.

New Drug Trial for FAP, Attenuated FAP and MAP

Adenomas, ranging in number from 10 to 100’s, develop in the gastrointestinal tract of patients diagnosed with familial adenomatous polyposis (FAP), attenuated FAP, and MYH-associated polyposis (MAP). Doctors regularly examine the colon for adenomas. Once the colon is removed, adenomas may still form in the remaining rectum or pelvic pouch. Adenomas may also form in the first part of the small intestine, just beyond the stomach. Two drugs called CPP-1X (eflornithine HCI) and sulindac may cause adenomas to shrink, either in the colon or duodenum.

A two-year randomized study has been approved by Health Canada to find out whether these drugs work better together or separately. Patients will be monitored every 3 months and will continue with their follow-up scopes. This study will be carried out at Mount Sinai Hospital under the direction of Drs. Steven Gallinger, Zane Cohen, and Robert Gryfe. For more information, please contact Registry Co-ordinator, Terri Berk, 416 586 4800 ext. 8334.

<table>
<thead>
<tr>
<th>Stage or Category</th>
<th>Size of polyp (mm)</th>
<th>Findings in the small intestine</th>
<th>Recommendation</th>
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<td>0</td>
<td>No polyps</td>
<td>Follow-up upper endoscopy in 5 years</td>
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<tr>
<td>2</td>
<td>1-2</td>
<td>Small polyp</td>
<td>Follow-up upper endoscopy in 3 years</td>
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<td>2.1-10</td>
<td>Medium polyp</td>
<td>Follow-up upper endoscopy in 6 months</td>
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<td>4</td>
<td>&gt;10</td>
<td>Large polyp</td>
<td>Endoscopic or surgical resection of polyp</td>
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Ostomy surgery involves the surgical redirection and elimination of body waste into an ostomy pouch system which is worn on the outside of the abdomen. This surgical procedure can be dramatic and may impact tremendously on the person’s and family’s daily lives and quality of life. For some people, the news that they may require an ostomy comes as a shock; for others, it signals relief from a threatening or debilitating illness.

Socially, the implications of having to manage one’s bathroom habits using an ostomy pouch can be a learning challenge which is emotionally frightening. In some hospitals, such as Mount Sinai, expert Enterostomal Therapy Nurses (nurses who specialize in the care of the ostomy), nurses, registered dietitians, psychiatric and chaplain support, and social workers are available to provide guidance and facilitate learning to care for the ostomy.

However, as the length of stay in hospital is becoming shorter with the intent of returning people to their home sooner, the ability for a person to learn “all they need to know” about their ostomy while in hospital is limited. As a result, some people may be discharged from hospital overwhelmed by their surgical experience and may require continued support to learn self-care. Family members may be asked to participate in care which requires additional teaching, understanding, and time. Certainly, some people may not be ready to assume this responsibility.

Ostomy care requires specialized knowledge, skill, and understanding of this often life-long condition. Recognizing the need to build capacity to manage this health care demand from hospital to community, the Rachel Flood Education Program is launching a certificate course, Advanced Ostomy Management for Healthcare Professionals, in March 2013. The program is incorporated within the Zane Cohen Centre for Digestive Diseases and the Gerald P. Turner Department of Nursing.

This comprehensive and unique distant, computer-based program was developed by experts who have expertise in caring for people who have ostomies: enterostomal therapy nurses; clinical nurse specialists; patient advisors; registered dietitian; social worker; and pharmacists. Each learning module focuses on a specific aspect of ostomy care.

Upon completion of this 12-week course, a one-week clinical development residency at Mount Sinai will follow. A certificate of completion will acknowledge that the Registered Nurse, Registered Practical Nurse, or other health care professional will have been prepared in advanced nursing and medical knowledge to provide the best in ostomy and patient-centred care to people and families. Our goal is to support the whole person and family toward self-managed ostomy care with dignity.
connects with the large intestine or colon. The absorption of food nutrients occurs mainly in the jejunum and ileum. The process of digestion and absorption is almost completed by the time food arrives in the colon. Thus, most material passing into the colon is waste.

The colon is 4 to 5 feet (1.2 to 1.5 metres) in length and slightly wider than the small intestine. It is divided into 5 sections.
- ascending colon
- Transverse colon
- Descending colon
- Sigmoid colon
- Rectum

The main function of the colon is to absorb water and minerals such as potassium and sodium, and to store waste until it is ready to be expelled by the body.

The rectum, the last portion of the colon, is shaped like an elongated pouch. When fecal material or stool moves into the rectum, special receptors are triggered causing a person to feel the urge to have a bowel movement.

The Healthy Digestive Tract

As we follow the digestive process, refer to the illustration of the digestive tract on the right. Digestion of food begins immediately in the mouth. Special proteins known as enzymes begin to digest the food so it can be used by the body.

When you are finished chewing and swallowing, the partially digested food passes through a tube called the oesophagus, into the stomach.

The stomach is a muscular pouch which churns and mixes the food into a semi-liquid form. Next the food passes into the small bowel, also called the small intestine.

Most of us have 22 to 25 feet (6.7 to 7.6 metres) of small intestine which is divided into three sections:
- the duodenum is 1 to 1.5 feet long (31 to 38 cm)
- The jejunum is 8 to 10 feet long (2.4 to 3 metres)
- The ileum is 12 to 15 feet long (3.6 to 4.8 metres)

The ileum, the last section of the small intestine,
Q: I was told to drink a lot while I have my temporary ileostomy but I really do not understand why. Can you tell me exactly how much is important every day? Does coffee and tea count? I actually ended up in hospital and was told I was dehydrated. What does that mean?

A: Being dehydrated means that your body does not have as much water and fluid as it needs. Signs of dehydration are: increased thirst, fatigue, decreased urine output, shortness of breath, stomach cramps, and light headedness. Most of the water you drink is absorbed in the large bowel. With an ileostomy the large bowel is no longer in use, so your body is unable to absorb as much fluid as it used to. As your body heals after surgery your remaining small bowel will adapt and becomes better at absorbing fluid. It is important to aim for at least 2 L of fluid per day, most of that being from water. Caffeine has a diuretic effect, so limit your coffee and tea to 2 cups (500 ml) per day.

Q: My husband has gained about 30 pounds since his bowel surgery. He likes to eat “comfort food” as he says it gives him less problems. What kinds of meals can I cook to help him be more healthy?

A: Comfort foods can get a bad reputation for being “unhealthy” but there are lots of ways to make these foods good for your body and soul. Choose leaner cuts of meat or poultry and trim any visible fat. Select low-fat dairy products or try non-dairy alternatives such as soy or almond milk. Add extra vegetables to brighten up your dish. And use herbs and spices to flavour foods without adding salt and butter.

Q: My son is 17 and has about 3 – 4 Cokes a day. Since his pouch surgery, he was reminded to avoid too much sugar. He complains of a lot of gas. Can you suggest how to help him cut down or cut out these sodas?

A: Sugar tends to draw water into the gut, speeding up transit time and causing more frequent bowel movements. One can of Coke has 8 teaspoons of sugar. Now multiply that by 3 to 4 cans and that’s a lot of sugar! Unfortunately, juice is not much better. One cup of 100% orange juice has over 5 teaspoons of sugar. The fizzy air in pop and carbonated waters can make you feel more bloated and gassy. The best way for your son to hydrate is with water, milk, or vegetable juices such as tomato or V8. To make water more exciting and flavourful try adding lemon juice, berries, cucumber slices, or fresh herbs.
Q: I have read different news reports about the dangers of red meat. Is it true that red meat causes cancer?

A: Research has shown that the more red meat and processed meat you eat, the higher the risk of developing some colorectal and stomach cancers. Eating more plant proteins such as beans and lentils have been shown to reduce the risk of some colorectal cancers. Reduce your meat intake by limiting red meat intake to 80 grams, about the size of a deck of cards, and making vegetables and whole grains the focus of your meal. Choose fish and poultry instead of red meat and try to have at least one vegetarian meal each week. Avoid eating charred meat or blackening meat and other foods because of harmful potentially cancer-causing chemicals.

Q: I had my bowel removed about 6 months ago and lost 15 pounds. I can’t seem to gain any weight although I have a good appetite. I am quite active and have started exercising. What kind of a diet can I follow?

A: Exercise is a healthy habit, but be sure to fuel your body before and after each workout. Approximately 2–3 hours before you exercise, drink fluid and try to eat a balanced meal including a grain such as crackers, pasta, rice or a potato, fruits and vegetables and a low-fat protein choice, such as chicken, beans, peanut butter or hummus. This will help to boost energy levels, prevent hunger, and keep you hydrated. After you exercise, have a shake (blend milk, fruit and ice together) or a cup of chocolate milk to store energy again, repair muscles, and fill up with fluids. Have a meal or snack soon after, including grains and protein such as chicken with rice and vegetables or pasta and meat sauce with salad. Other healthy foods that have more calories or bang per bite are: avocados, smooth nut butters, granola bars, pastas, bagels, Greek yogurt, cheese, and oils such as olive and flaxseed oil.

It is important to try to get a variety of foods in your diet. If you’re scared to eat new foods, start with a small amount and gradually increase. Your tolerance may be related to how much you eat and how well you chew.

Q: My wife and I are planning a trip to Mexico to celebrate after my bowel operation. I am a little worried about my diet and what I need to watch when travelling. Any tips you might have would be great.

A: If your bowel operation was more than 6 weeks ago, you should be back on track to eating your usual diet. If there are foods you haven’t had since surgery that you plan to have, such as pineapple or berries, I suggest you give them a try before you go to see how you tolerate them. When introducing any new foods, start with a small amount and chew very well. Mexico’s bright sun and heat will likely cause you to sweat. Make sure you are staying hydrated with lots of water. If you have an ileostomy or pelvic pouch, be sure to add some salt to your food. Lastly, the most important tip is to relax and enjoy yourself!
Meet and Greet

As a multidisciplinary Registry, we offer many different services to patients and their families. We would like to introduce you to team members who have recently joined us.

**Dr. Sarah Ferguson** is a gynaecologic-oncologist at Princess Margaret Hospital (PMH) and an assistant professor at the University of Toronto. Dr. Ferguson has a keen interest in screening and prevention of hereditary gynaecologic cancers. She spearheaded a study in 2009 to determine how common Lynch syndrome was among newly diagnosed endometrial cancer patients at PMH. Lynch syndrome was identified in some of these women, and action was taken to prevent additional cancer (such as colorectal cancer) in this group and their family members. In addition, Dr. Ferguson is designing a gynaecological cancer screening protocol for women with Lynch syndrome, to provide services to carriers and assess the effectiveness of screening techniques.

**Dr. Jordan Lerner-Ellis** joined Mount Sinai Hospital as the new Director of the Laboratory for Advanced Molecular Diagnostics in 2011. He is also an Assistant Professor at the University of Toronto and is an Associate at the Ontario Institute for Cancer Research. Before joining our team, Dr. Lerner-Ellis completed his PhD at McGill University in 2005 and completed the Clinical Molecular Genetics training program at Harvard Medical School. He is working on exciting projects to increase our understanding of hereditary gastrointestinal cancer. His next project will use new technology to analyze all the genes in families that have an unsolved hereditary condition, looking for new genes that may be involved in cancer development.

**Dr. Anand Govindarajan** is a gastrointestinal surgical oncologist at Mount Sinai Hospital and Princess Margaret Hospital, and an assistant professor in the Department of Surgery at the University of Toronto. He has an interest in familial gastrointestinal malignancies, including hereditary forms of stomach and colorectal cancer. Currently, he is coordinating a study examining quality of life and cancer-related worry in families of patients who are at risk of familial forms of gastrointestinal cancers. This is a large unmet need in these families which the results of the study may help address. He is also examining the frequency and types of other cancers to help develop evidence-based screening recommendations in these high-risk families.

**Dr. Sanjay Murthy** is a gastroenterologist working out of Mount Sinai Hospital. He has received subspecialty training in inflammatory bowel disease as well as diagnostic and therapeutic endoscopy. He has a particular interest in colorectal cancer prevention in high-risk groups, including those with hereditary cancer syndromes such as Lynch syndrome and FAP. His primary focus is in the application of newer endoscopic methods for detection and treatment of precancerous lesions in these conditions. His future work seeks to evaluate factors associated with accelerated cancer development.
Frances Nippalow obtained her Medical Administrative Diploma from Humber College in 1995. In November 2012, she joined our centre. Frances will be supporting the Genetic Counselors as well as creating family trees, keeping consent forms up-to-date, and general administrative tasks. We welcome Frances to our team.

Jennifer La obtained her Bachelor’s in Science from University of Guelph in 2009 and joined our centre in 2011. She is the voice that you will hear when you call our office, and she will be the first one to greet you when you come in.

In October 2012, several staff from the Familial GI Cancer Registry attended the 16th Annual Meeting of the Collaborative Group of the Americas on Inherited Colorectal Cancer in Boston. This meeting is a great opportunity for different groups who study hereditary gastrointestinal cancer and polyps to discuss their latest research and to learn from each other. Since hereditary cancer syndromes are rare, these meetings promote research collaboration and sharing of information and knowledge.

Despite encountering Hurricane Sandy during the meeting, several members of our team presented talks and posters on a variety of topics, such as interpreting new and rare genetic changes in Lynch syndrome, educating others on a rare hereditary condition known as biallelic Lynch syndrome (see separate article), and reviewing our research on cancer risks in Lynch syndrome. The meeting was informative and included sessions on a variety of relevant and thought-provoking topics. Our group does its best to stay abreast of, and contribute to, the latest research on hereditary colorectal cancer and polyposis.
**Adenoma:** A precancerous polyp.

**Biallelic:** Two copies.

**Colorectal:** Large bowel and rectum.

**Duodenum:** First part of the small intestine.

**Dysplasia:** Change of size, shape, organization of tissue.

**Endometrium:** Lining of the uterus.

**Enterostomal Therapy Nurse:** Nurse specializing in the care of the ostomy.

**Esophagogastroduodenoscopy:** The insertion of a fibreoptic flexible tube to examine the windpipe, stomach, and first part of the small intestine.

**Familial Adenomatous Polyposis:** Genetic disorder of the gastrointestinal tract characterized by 100 or more precancerous polyps of the colon.

**Lynch Syndrome:** Genetic disorder in which people are at increased risk of cancer of the large bowel, endometrium, and other associated cancers.

**Mismatch Repair Genes:** Genes that detect and repair “spelling” mistakes that occur during DNA replication.

**MYH-Associated Polyposis:** Genetic disorder of the gastrointestinal tract characterized by 10 or more precancerous polyps in the colon.

**Mutation:** A change or fault in a gene which occurs when DNA is being copied so that a slightly different gene is formed. This change is preserved and copied identically thereafter.

**Ostomy:** Surgical redirection and elimination of body waste into a pouch system which is worn on the outside of the abdomen.

**Pelvic Pouch:** Removal of the large bowel and lining of the rectum, leaving the underlying anal muscles. The last part of the small intestine is joined to the anus and an internal reservoir is created in the pelvis.

**Randomized Trial:** Patients are put into a group by chance according to a computer program.

**Serrated Polyposis Syndrome:** Genetic disorder characterized by hyperplastic polyps of the colon, depending on number, size, and location, which may be associated with an increased risk of colon or gastric cancer.

**Whipple Procedure:** Major surgery involving small part of stomach, gallbladder, pancreas, duodenum, and part of jejunum.