Introduction to a New Series: 
Practical Approaches to 
the Diagnosis and Treatment 
of Colorectal Cancer

For the past twenty years it has been my privilege to coordinate and present the Series “Colorectal Cancer” (CRC) for this Publication. Over this period there have been great strides made in the understanding, diagnosis, screening, follow up, and treatment of this, one of the most common sites, of malignancy.

The many contributors to this series have provided insight and practical information for the practicing clinician. Now it is time to turn the task of coordinating and presenting each symposium to another and in this regard I am very pleased that Dr. James Disario has agreed to continue this CRC series in future publications. But first, I am proud that this present collection of nine articles represents a landmark in the series and places many of the advances and questions about colorectal cancer into prospective.

The genetic factors of practical importance alluded to in the initial series (1) have been further defined and put into workable models. The human genome has been completely mapped and a variety of cancer genomes have been identified. The research that has gone forth in this area of genetics now brings new tools and practical alternatives to physicians confronting these problems and to their patients. Genetic testing can discover mutations that allow individuals to be identified with the risk of a continuously increasing variety of colorectal cancer syndromes.

It is important to review and understand the genetics involved. The outstanding lead article in this series by the physician son and father team of Jordan and Gary Hoffman serves as a primer for understanding the complicated alphabet, concepts, and value of the genetics. It sets the stage for the three articles that follow and will offer the background that the reader can utilize to understand the practical benefits of genetic testing. It should be available for quick reference as the reader proceeds through the series. Keep in mind, there is more to come as the investigations into the genetics of all colon cancer continues to identify additional genes.

The clinician, primary care physician, gastroenterologist, or surgeon who is at the early phase of diagnosis, is in position to offer a valuable service to both the patient and to the family members. The
identification of a carrier or non-carrier state has major clinical importance for surveillance and management. It is no longer an option but an obligation to identify individuals at risk. How best and on whom to do this is discussed in the following two articles.

Drs. Samadder and Burt from the prestigious Huntsman Cancer Institute at the University of Utah discuss “Who to Send for Genetic Testing” followed by Marjan Champine’s valuable presentation of the “Role of Genetic Counselors and Gastroenterologists.” These articles, taken together, in conjunction with the submission from this center in the previous issue of this series (2) and the detailed review by Lynch et. al (3) serves as a guideline for the clinician facing these problems. Emotional issues evolve and must be addressed. Unfortunately the results of genetic testing are not always clear cut and “non-diagnostic” results need to be placed in perspective for the medical and economical ramifications that follow. Numerous algorithms are available for diagnosis and management but individual evaluation is best done under the purview of the expert. It is important to remember that when tumor tissue is available, the genetic testing procedures (and algorithms) are more easily and economically carried out. However when the guidelines for suspicion of a familial colon cancer condition are followed and tumor tissue is not available, then testing blood is possible with a high degree of specificity and sensitivity. This process at present however is both time consuming and expensive and should be under the direction of the genetic specialists. Links to an excellent online resource that is funded by the NIH are available: www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=fap
These provide information on how to make a clinical diagnosis, how to execute genetic testing to confirm the diagnosis, and how to manage an individual once diagnosed with the genetic disease. There is also a listing of laboratories that offer genetic testing related to the specific genetic condition.

The following article by William Hendricks and Daniel Edelstein from Johns Hopkins University takes genetic information a step further by demonstrating how the “genomic data” can be utilized “to assess risk, predict outcomes, and individualize treatment” in patients with colorectal cancer. The potential success (or failure) of certain oncological therapies can be predicted through the use of genetic tumor (and hopefully blood based) testing procedures. This approach has value for both improved patient survival as well as decreasing the discomfort and economic burden of standard therapy.

We switch gear in the next four articles in this series by returning to the interrelated concepts of screening, surveillance and detection. Much advancement has been made in our understanding and implementation of these concepts both technically and with controlled trials that demonstrate efficacy. Screening for colorectal cancer is not a choice between fecal occult blood testing and colonoscopy. New tests are emerging that provide options but there remain many unanswered questions. In addition it is estimated that about one-third of the eligible individuals in the United States do not participate in any screening program.

It is nearly twenty years since the publication of the landmark National Polyp Study (4). The continued accumulation and analysis of follow up data has generated a wealth of valuable clinical information (5,6). Nevertheless the job is not finished. Screening methods continue to evolve, new information impact on the performance of established procedures and controversy exists.

The prominent group from the Thomas Jefferson University in Philadelphia, PA has reviewed the vast and varied International Colorectal Cancer Screening Programs. There is near universal agreement in the need to screen but the question is how. Their review is enlightening for the individual responsible for designing or recommending a screening program. The major problem with screening is to devise a program that maximizes the screening effort. It is obvious that to maximize screening, some form of direct patient contact is necessary, as simply providing screening alone does not work.

The use of fecal occult blood testing (FOBT) continues to be an integral part of worldwide screening programs. The advantages and limitations of the newer technology of fecal immunochemical testing for hemoglobin (FIT) have previously been reviewed in this series (7) and FIT is replacing FOBT in many programs. Problems with both of these approaches to stool testing continue to exist though progress in standardizing the reporting of FIT is moving forward as is reported in the concluding article of this series by Dr. Graeme Young. The real hope however for a reliable, inexpensive and easy to use method for screening, “the Holy Grail of cancer detection” (8), has been the development of a blood-based test. The article by Catherine Lofton-Day continues (continued on page 22)
of Epigenomics, a molecular diagnostics company developing products for the screening and diagnosis of cancer, reviews the progress made in this field both in the United States and Europe. The genetics of colorectal cancer that we have learned so well in the previous articles are again of paramount importance in the development of these blood-based tests. So far, the value of these blood-based tests has been with invasive cancer. The use for detection of advanced adenomas is not yet ready for prime time but there is hope and progress.

Despite poor compliance rates, our discussions of screening and colon cancer prevention should not imply that everything is rosy when screening is instituted. Flexible sigmoidoscopy, fecal occult blood testing, and radiological techniques alone or combined all have their drawbacks. In many areas of the world, colonoscopy is deemed to be the most effective method for screening and is particularly attractive as it incorporates cancer prevention through the removal of adenomatous polyps. Recent data on risk reduction however has questioned this concept, particularly for lesions located in the right side of the colon that may be flat and easily missed. The article by Drs. Coe and Wallace from the Mayo Clinic in Jacksonville, FL is a good review of flat colonic lesions, their pathology and clinical significance. The important concerns of how to minimize the risk of missed lesions treat the lesions when found, and provide appropriate follow-up are addressed.

The risk of right colon lesions as well as the entire concern about screening and removal of colon polyps is placed into perspective in the next provocative article by Drs. Allison and Meijer. To effect balance, the authors suggest that options other than colonoscopy for screening, such as FIT, could be a better option for mortality reduction from colorectal cancer. It seems that the net balance from these discussions leaves the responsibility to the physician that confronts the patient. Compliance with, risks, availability and quality of performance, must all enter into the decision process.

The World Endoscopy Organization’s (WEO) prestigious Colorectal Cancer Screening Committee is chaired by Professor Graeme Young of Flinders University in Adelaide, Australia. The final article in this series comes from Dr. Young who has been a valuable contributor to the many issues of this series. Under his leadership the WEO committee has addressed these and many of the other important issues related to the diagnosis and treatment of colorectal cancer. His article in this series is a report of the Committee’s Workshop that was held in 2011 as they relate to the issues discussed in this series. The ongoing progress in the development of new molecular markers and how these might impact of the right colon lesion problem is presented. Additional areas addressed by this Committee are the choice of screening test, how many and what kind of tests, and follow-up algorithms. This Committee, under the auspices of the WEO has developed a list of issues that will be considered for Working Parties to address. The issues considered are:

1. The challenge of right-sided lesions
2. Surveillance intervals
3. Reporting standards for FIT tests
4. Comparing new tests
5. Comparative effectiveness screening trials of different strategies
6. Sample stability and quality
7. Cost effectiveness including age for screening
8. Improving population engagement with screening
9. Quality assurance for organized screening programs
10. The adenoma as a target lesion

The WEO Committee indicates that significant changes are expected in how screening will be performed in the future. We look forward to future issues of this Colorectal Cancer Series in Practical Gastroenterology under the direction of Dr. James Disario.

References
1. Levin, B: Colorectal Cancer: Genetic factors of practical importance. Practical Gastroenterol. 1992, XVI, No1: 16G-16H.