



Patient Report

Heritable Colorectal Cancer Syndromes

Reporting on an article, *Heritable Colorectal Cancer Syndromes: Recognition and Preventive Management*, by Dr. Lisa Boardman of Mayo Clinic

A Report by
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For those who aren't familiar with USA medical history or geography, I'll give a bit of background. Our rather short history (our country is just over 200 years old), rather mobile population and rather disorganized health care system have made it difficult to find and follow people with any condition. PJS is more difficult than most for several. There haven't been many registries to track PJS folks, nor do most of us need continuous or intensive medical care. We move, change doctors, misplace medical records. It's hard enough for us to keep track of ourselves and even harder for our institutions to keep track of us.

Mayo Clinic¹ has a unique history with PJS folks because of its location and history. Located in America's heartland, many patients and families with rare and/or serious conditions are followed there for years. Also, according to the OMIM, "The designation Peutz-Jeghers syndrome appears to have first been used (at least in the title of an article) by Bruwer et al. (1954) of the Mayo Clinic."² So, they have been following PJS folks for a long time.

In 1957, Dr. Bartholomew et al. of Mayo Clinic wrote about their six cases of PJS and reviewed the total reported in the literature, 75.³ In a second article by the group, published in 1962, the authors report a total of 182 cases including 8 new ones at Mayo Clinic.⁴ This article is the basis for many estimates about PJS including incidence (1 in 200,000) and location of polyps (96.2% in small intestine, 30.8% in rectum, 29.1% in colon, 24.2% in stomach and 2.7% in appendix). They also noted that age at time of diagnosis ranged from 2 to 82 years and averaged 24.3 years, and that PJS affected both sexes equally. Interestingly, though this article was published in a gynecology and obstetrics journal, they made no mention of any reproductive problems associated with PJS.

The authors did discuss malignant potential of PJS polyps, "Ten of 12 patients seen at the Mayo Clinic have been observed for a total of 124 years - range 2 to 29 years, average 12.4 years - since treatment was initiated for this syndrome or from the time adequate surgical specimens have been available for study. None of these patients to date have shown any evidence of malignant transformation. Three patients have died: 1 from an intestinal deficiency syndrome following extensive resection of the small intestine, 1 from massive gastrointestinal bleeding associated with hundreds of gastrointestinal polyps, and 1 from myocardial infarction at age 82 with the diagnosis of polyposis being made at necropsy. The 8 patients in the family reported on herein have been observed closely for periods totaling 100 years, ranging from 1 to 22 years with an average of 12.5 years, without evidence of malignant transformation in the intestinal polyps having been found."

If only the trend had continued. Unfortunately, those eight patients in one family were the Harrisburg family reported by Dr. McGarrity and others in 1988 (See my report: *Doctors Peutz and Jeghers and Their Patients*) who noted: "Their 12 affected family members comprise the largest Peutz-Jeghers kindred reported. The course of this family illustrates that Peutz-Jeghers syndrome is not a benign disease. One family member developed a duodenal carcinoma in a hamartoma with adenomatous changes; this progression in the duodenum has not previously been reported. Ten patients underwent 75

polypectomies. One patient developed short bowel syndrome. Three patients died in young adulthood. The development of gastrointestinal malignancy in 2 of 12 affected patients suggests that Peutz-Jeghers syndrome may be a premalignant condition."

In 1998, Dr. Lisa Boardman⁵ reported a greatly increased risk of cancer in PJS.⁶ As I noted in a previous report, *An Important PJS History*, she "reviewed the cases of 34 PJS patients seen at Mayo Clinic between 1945-1996, that an increased risk of cancer in PJS was found -- a relative risk of 18.5 times the general population for women and 6.2 times for men. There were 16 cases of cancer in 34 patients: 10 cases of GI cancer and 6 cases of extraintestinal cancer."

Dr. Boardman has continued her PJS studies and in a 2000 article reports several more cases of cancer in people with PJS.⁷ Dr. Boardman collaborates with Dr. Stratakis of the NIH and communicates with other PJS specialists including Doctors Amos, McGarrity and Giardiello. She reviewed the GeneClinics PJS entry and her 1998 findings are included therein.⁸ It is likely that some of the new reports of cancer in her 2000 article are from sources other than Mayo Clinic records.

Last month a new article by Dr. Boardman was published in *Gastroenterology Clinics of North America*. She discusses the four main hereditary colorectal syndromes: hereditary nonpolyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), juvenile polyposis syndrome (JPS) and Peutz-Jeghers syndrome (PJS). I'll skip right to the PJS section and note that she does accept Dr. Giardiello's cancer risk estimates (See my report: *Very High Risk of Cancer in Familial Peutz-Jeghers Syndrome*) and a similar screening program.

I keep hoping we'll be let off the hook, that somehow the PJS-cancer risk estimates will reverse to the low levels projected in the 1960's. But this is not to be. Two years after Dr. Giardiello's article the screening schedule is still rigorous.

Here is what she wrote:

"Though the multiple organ systems at risk for cancer in Peutz-Jeghers syndrome make for a rigorous, sometimes cumbersome, surveillance program, the finding in a recent meta-analysis that the risk in the colorectum, breast, gynecological tract, stomach, and pancreas equals that in other high-risk conditions supports the needs for cancer surveillance in this population.¹⁰ Gastrointestinal tract evaluation beginning at age 10 may be accomplished with biennial upper endoscopy and small bowel radiography. Colonoscopy may be initiated in early adulthood and continued at least biennially to achieve and maintain polyp clearance. Early detection of pancreatic cancer with either endoscopic or transabdominal ultrasonography should begin at 30 years of age. Though breast and reproductive cancers cannot be prevented, early detection is recommended for women with biennial mammography, annual pap smear and annual pelvic ultrasound or endometrial biopsy beginning at age 20. Sex cord tumors with annular tubules may be detected at

pelvic ultrasonography but do not routinely require medical or surgical therapy. To evaluate for Sertoli cell tumors, boys 10 years of age and older may undergo testicular examination. Testicular ultrasound may be added to this screening regimen if precocious puberty or feminization develops."¹¹

You can see by Dr. Boardman's references that she relies heavily on Dr. Burt's screening guidelines. Dr. Burt is at the Huntsman Cancer Institute in Salt Lake City, USA. In October 2000, we saw an earlier version of these guidelines. The only change in this newer article¹¹ is that he has added the possibility of uterine washings to pelvic exams for women. Now: Annual pelvic examination with pap smear; and annual pelvic or vaginal ultrasound and/or uterine washings, both start at age 20 years.

By the way, both Dr. Boardman and Dr. Burt use the 1 in 200,000 estimate for frequency of PJS.

These rigorous screening guidelines are close to those set out in the Johns Hopkins PJS booklet¹², with some adjustments for ages of beginning scopes, x-rays, pelvic exams and mammograms. It should be noted that Dr. Giardiello et al., authors of *Very High Risk of Cancer in Familial Peutz-Jeghers Syndrome*, are at Johns Hopkins and influenced this booklet.

This historical and geographical look at PJS gives us an indication of what's expected of us: screening, screening and more screening. Our discussions reveal that different doctors have different plans. Perhaps those in the group who'd like stricter screening can use the guidelines from these major medical institutions to persuade doctors and insurers to perform them.

Remember: I am not a medical professional, but a patient observer. Take all questions to your doctor. And if you don't get satisfactory response, seek a second opinion.



¹Mayo Clinic, Rochester, Minnesota -- <http://www.mayoclinic.org/rochester/>

²Bruwer, A., Borgen, J. A., Kierland, R. R. *Surface pigmentation and generalized intestinal polyposis (Peutz-Jeghers syndrome)*. Proc. Staff Meet. Mayo Clin. 29: 168-171, 1954.

³Bartholomew, L. G., Dahlin, D. C., Waugh, J. M. *Intestinal polyposis associated with mucocutaneous pigmentation (Peutz-Jeghers syndrome)*. Gastroenterology 32:434-451, 1957.

⁴Bartholomew, L. G., Moore, C., Dahlin, D. C., Waugh, J. M. *Intestinal polyposis associated with mucocutaneous pigmentation*. Surg. Gynec. Obstet. 115: 1-11, 1962.

⁵Boardman photograph -- <http://www.mayoclinic.org/gi-rst/11547901a.html>

⁶Boardman LA, Thibodeau SN, Schaid DJ, Lindor NM, McDonnell SK, Burgart LJ, Ahlquist DA, Podratz KC, Pittelkow M, Hartmann LC. *Increased risk for cancer in patients with the Peutz-Jeghers syndrome*. Ann Intern Med. 1998 Jun 1;128(11):896-9. PMID: 9634427 [PubMed - indexed for MEDLINE]

⁷Boardman LA, Couch FJ, Burgart LJ, Schwartz D, Berry R, McDonnell SK, Schaid DJ, Hartmann LC, Schroeder JJ, Stratakis CA, Thibodeau SN. *Genetic heterogeneity in Peutz-Jeghers syndrome*. Hum Mutat. 2000;16(1):23-30. PMID: 10874301 [PubMed - indexed for MEDLINE]

⁸<http://www.geneclinics.org/profiles/pjs>

⁹Boardman LA. *Heritable colorectal cancer syndromes: recognition and preventive management*. Gastroenterol Clin North Am. 2002 Dec;31(4):1107-31. PMID: 12489281 [PubMed - in process]

¹⁰Giardiello FM, Brensinger JD, Tersmette AC, Goodman SN, Petersen GM, Booker SV, Cruz-Correa M, Offerhaus JA. *Very high risk of cancer in familial Peutz-Jeghers syndrome*. Gastroenterology. 2000 Dec;119(6):1447-53. PMID: 11113065 [PubMed - indexed for MEDLINE]

¹¹Burt, RW. *Polyposis syndromes*. Clin Perspectives Gastro 2002;51-9

¹²www.macgn.org/PDF/pjs.pdf

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