# Appendix Cancer Awareness Month

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**Becca Battisfore:**

Welcome to the latest edition of the College of American Pathologist CAPcast. I'm Becca Battisfore, Content Specialist with the CAP. In this episode, Doctors Edgerton and Hagen will be talking about appendix cancer.

August is Appendix Cancer Awareness Month. This is a rare cancer diagnosed in approximately three to four people per million per year. Between 2000 and 2016, it has been reported that there's been a 232% increase in appendix cancer in the United States. Given this rapid increase, it's important that clinical teams have access to the most accurate and complete pathology reports of malignant tumors through the CAP'S cancer protocols. Before we get into the questions, let's learn more about our guests. Dr. Edgerton, please introduce yourself.

**Dr. Mary Edgerton:**

So, I'm Dr. Mary Edgerton. I am certified in AP and CP and also in clinical informatics. So, my interest with the Cancer Protocols comes not only from diagnosing cancer, but also in seeing that the data is able to be collected directly from the reports and transmitted electronically. And we'll talk about that and its impact a little bit later. I most recently was at the MD Anderson Cancer Center, and I retired after working there for 17 years. But what pathologist ever retires? I'm at the University of Nebraska.

**Becca Battisfore:**

Great. And Dr. Hagen?

**Dr. Katie Hagen:**

My name is Katie Hagen. I'm a pathologist practicing at Mayo Clinic in Rochester, Minnesota, and I subspecialize in gastrointestinal pathology.

**Becca Battisfore:**

Great. Thank you both for joining the podcast today, Dr. Edgerton, I'll let you take it from here.

**Dr. Mary Edgerton:**

So, I have to say I knew the appendix as appendicitis and my rule of thumb was if you see eosinophil, submit the whole thing and look for parasites. I don't think I ever actually saw an appendiceal carcinoma, although I did see pseudomyxoma peritonei once. Can you tell us a little bit about appendiceal carcinoma? It's so rare, but there has been this odd increase.

**Dr. Katie Hagen:**

Yeah, that's interesting. I think data has shown that it has increased remarkably in the past several decades. But as we heard in the introduction, it's still relatively rare, occurring approximately in three in 1 million individuals, so not something we see very commonly. And the appendiceal carcinoma tends to be kind of unique from other GI cancers that we see. In particular, there are unique entities, LAMN and HAMN, which can lead to a unique entity pseudomyxoma peritonei. And this is something we usually don't see with other GI malignancies.

**Dr. Mary Edgerton:**

So, that's fascinating. I have to say, when I was at MD Anderson, I was across the hall from a GI pathologist, and every year we had new surgical pathology fellows started to sign out with us, new subspecialty fellows. And I heard about LAMN and HAMN and I thought, "Ah, this is fascinating." I mean, what wonderful names LAMN and HAMN. Can you tell us a little bit more about what LAMN and HAMN are and how they've changed the diagnostic practice in appendiceal tumors?

**Dr. Katie Hagen:**

As I mentioned, LAMN and HAMN are something that are kind of unique to the appendix. So, low-grade appendiceal mucinous neoplasm, LAMN, and high-grade appendiceal mucinous neoplasm, HAMN. Compared to conventional adenocarcinoma, these tumors kind of have a pushing border of invasion as opposed to conventional adenocarcinoma, which is comprised of kind of these infiltrative malignant glands that destroy the wall of the appendix. The low-grade version, LAMN, has low grade cytologic features, while HAMN has high-grade cytologic features. As I mentioned, these can lead to the development of pseudomyxoma peritonei, and so what that entity is is when you have an accumulation of mucin and tumor cells within the abdominal cavity. And so this is how these tumors LAMN and HAMN typically spread, whereas conventional adenocarcinoma often metastasizes to lymph nodes or other organs.

**Dr. Mary Edgerton:**

I do recall as a resident getting a case of pseudomyxoma peritonei, and the question I asked my attendings was, "Is this going to be a continuing problem? Are they constantly going to have to go in and scrape her abdomen?" So, how is it treated, and can the risk of recurrence be eliminated?

**Dr. Katie Hagen:**

Unfortunately, these do kind of tend to be slowly progressive entities. They can be managed clinically. With low-grade disease, oftentimes these patients will undergo tumor debulking and they might undergo something called HIPEC, which is heated intraperitoneal chemotherapy where the clinicians directly infuse chemotherapy into the abdominal cavity. Sometimes with high-grade disease, the patients may also receive systemic chemotherapy, but that HIPEC procedure is pretty unique to treating this kind of pseudomyxoma peritonei. And it can keep the disease under control, but usually this is kind of, as I mentioned, a slowly progressive disease.

**Dr. Mary Edgerton:**

Yes, I do remember, and that was over 20 years ago, that that was the prognosis for the patient. But I presume this treatment does improve, at least the quality of life.

**Dr. Katie Hagen:**

These patients can survive decades and unfortunately do have to deal with this disease, but it can give them a better quality of life.

**Dr. Mary Edgerton:**

So, how is appendiceal carcinoma detected? Is it not seen until it's burst through the appendix because there's otherwise no screening for it?

**Dr. Katie Hagen:**

Yes, because this is such a rare entity, we don't currently have any screening protocols for appendiceal adenocarcinoma, and it usually is detected incidentally. So, a patient might present with abdominal pain and maybe have a suspected appendicitis, undergo an appendectomy and we see the cancer there. Or perhaps the patient might have some sort of imaging in which the tumor is identified. Or in worst case scenario, the appendix has burst and kind of seeded the abdomen with the pseudomyxoma peritonei.

**Dr. Mary Edgerton:**

Have there been any molecular developments in terms of understanding the genesis of appendiceal carcinomas and these mucinous tumors?

**Dr. Katie Hagen:**

Studies have shown that GNAS mutations and KRAS mutations are pretty common in appendiceal adenocarcinoma. Interestingly, even though the appendix is in very close proximity to the colon, it seems to have a unique pathway from the colon in terms of carcinogenesis. We know some common mutations that are seen in colorectal cancer like APC, p53, BRAF, and microsatellite instability, these are not actually seen very commonly in appendiceal carcinomas. So, I think there's still a lot to be learned about appendiceal carcinoma and its molecular pathogenesis, but it does seem to follow a different pathway from colon cancer.

**Dr. Mary Edgerton:**

Well, that is interesting. And being rare, I'm sure that makes it all the more difficult to have enough cases to study. So, in that vein, we know that the electronic Cancer Protocols actually help to store data from cases, so that not only is it reported to cancer registries in a timely fashion and is helpful in terms of looking at these abnormal increases in incidents, but it also helps to identify cases if you intend to try to perform more molecular studies. How does using the electronic Cancer Protocols help your practice?

**Dr. Katie Hagen:**

I think the Cancer Protocols are a really great tool. It really makes it easy for us to report in a standardized fashion and make sure we include all these important prognostic elements in the reports. I can also rest at ease that I am including all the information that the treating clinicians need in their reports to provide the best patient care. So, I think these are really great tools for us as pathologists.

**Dr. Mary Edgerton:**

I have to imagine that that's probably helpful, especially in something like appendiceal cancer that comes up infrequently and you have to remember everything that you need to report. So, it's easier to pull up a checklist. We used to call it the checklist, but we now call it the Cancer Protocols. To pull that up and be able to say, "Oh yes, I reported on everything. I don't need to go back to this case and look this up." Is that the case, and in teaching also?

**Dr. Katie Hagen:**

Yes, definitely. It really serves as that checklist, as you said. And there's many different GI tumors and it's hard to remember all of the important elements for each individual organ system, and this just really makes it easy to make sure you're including all the right elements.

**Dr. Mary Edgerton:**

That's great. And I guess the appendiceal tumors are rare enough that it doesn't make sense to do a prophylactic appendectomy?

**Dr. Katie Hagen:**

No, and I think, as I mentioned, the genetics of appendiceal cancer is still being studied, so currently prophylactic appendectomies is not something that is routinely done.

**Dr. Mary Edgerton:**

Yes, I work a lot in breast pathology where, as you know, we have a lot of prophylactic surgeries, but we are much further along in terms of identifying genes that have a high penetrance for the eventual development of invasive carcinoma. So, this has been fascinating. I've learned about LAMN and HAMN, and I'm updated on how pseudomyxoma peritonei or as it's commonly referred to, jelly belly, is treated. And thank you for that. And do you want to say anything else about the field and using the Cancer Protocols? We know it's Appendix Carcinoma Awareness Month.

**Dr. Katie Hagen:**

I guess I would just briefly like to mention the staging system for LAMN, as it is pretty unique compared to other GI cancer staging systems and relatively new as well. So, I guess this staging system consists of a Tis, T3 and T4. So, we don't have a T1 or T2 like we do for other GI malignancies. And I think collecting data specifically on the T3 LAMNs will be very important because we don't really know if they behave more like a Tis, which could be cured with appendectomy, or if they'll behave like a T4 tumor where those patients are at risk for developing the pseudomyxoma peritonei and need to be followed. So, I think in particular, collecting more data on these T3 lesions will be important to see how these patients progress or don't progress, and also if we should continue to use this unique staging system for LAMN.

**Dr. Mary Edgerton:**

So, going a little deeper on that, Tis is the [inaudible], and that's above the basement membrane has broken through. What distinguishes T3 and what distinguishes T1?

**Dr. Katie Hagen:**

So, Tis in this case can actually be if the tumor is pushed into the submucosa or up to the muscularis propria, and as I mentioned, it's kind of unique for the appendix. I guess in other organs that would be considered T1 or T2, but we group this all into Tis for LAMN in the appendix. Once the tumor has pushed through the muscularis propria into the periappendiceal adipose tissue, that would be considered T3. If the tumor has spread to the serosal surface, then that would be considered T4. And interestingly for LAMN, it's either the mucin or the tumor cells, whichever has spread furthest. So, that's a little unique for appendiceal cancers as well.

**Dr. Mary Edgerton:**

So, that can be a cellular mucin, just the presence of mucin alone?

**Dr. Katie Hagen:**

Correct. Yes.

**Dr. Mary Edgerton:**

And certainly that's different from the breast where if we see mucin alone, we particularly in a biopsy would say mucocele versus invasive mucinous carcinoma, and they have to go back and do a more definitive excision for diagnosis. But mucin alone doesn't constitute a tumor presence for breast. That's fascinating. When I went into pathology, one of my mentors said, "The fun thing about pathology is you can keep learning the rest of your life, you'll see something new no matter how old you are or how long you've been in practice."

**Dr. Katie Hagen:**

Yes, it's definitely a great field and always learning something new.

**Dr. Mary Edgerton:**

All right. Well, out there for those listeners who might be thinking of pathology, medical students, early residents, that's why we do it. It excites us for the rest of our lives. And if you're dealing with cancer, using the electronic Cancer Protocols really helps to improve patient care by completeness and to improve patient care for the future by providing a record of cases, especially in these very rare tumors. So, you can find links to the Cancer Protocols that were mentioned in this episode. You can find these links at the cap.org, that's cap.org website. And if you're a member, they're in the MyCAP app, which I find very useful. Thank you very much, Dr. Hagen, and thank you.

**Dr. Katie Hagen:**

Thank you. This has been great.