

[MUSIC PLAYING]

**SALLY E.** OK. So I'm going to talk about the management of concomitant thyroid and parathyroid disease. And just to get everybody in the groove, that's if you have thyroid disease that requires surgery, do you also have hyperparathyroidism? That's one side of it. And then, it's if you have primary hyperparathyroidism, do you also have thyroid disease? That's the other side of it.

So we're going to talk about the second situation first, because it's more defined in the literature. This is the AAES Parathyroidectomy Guidelines which was basically my fourth child here, and which came out in the summer of 2016. And it was an online supplement that was 174 pages long, full of pearls and recommendations and tables and supporting all the supporting evidence for the drastically-condensed executive summary that appeared in *JAMA Surgery* and then was picked up and also appeared in *JAMA*. This slide is intended to remind me to remind you that our own Mitch Tublin of radiology was one of the 16 coauthors on the Parathyroidectomy Guidelines, which also included Shonni Silverberg of endocrinology and Sylvia Asa of pathology and 14 endocrine surgeons. It was really fun, took three years.

So here's the abstract from the Parathyroidectomy Guidelines, and the abstract concisely states the sensible data supported and sensible revolutionary data supported recommendations that the authors made. One of them, which is not revolutionary, is that cervical ultrasound or other high-resolution imaging is recommended for operative planning when you have hyperparathyroidism. And another one pertinent to this talk-- which will only be 15 minutes, by the way. I'm going to try to make up the time that we're a little behind-- is that clinically-relevant thyroid disease should be assessed preoperatively and managed during parathyroidectomy routinely. So find out about it and take care of it at the same time that you're doing the parathyroid surgery.

And what you want to keep in mind here is this range of probability. In patients with primary hyperparathyroidism, there is concomitant thyroid disease in about 40% of people, and I'll say that 40% again, and if I don't please remind me. Concurrent-- this is text from the guidelines-- concurrent Thyroidectomy, Tx, may be needed for thyroid disease that requires resection during parathyroid surgery or for suspicion of parathyroid cancer. You do onc block resection, or to remove an abnormal intrathyroid parathyroid or to improve access is a legitimate reason to take out that half of the thyroid, if necessary.

And these four recommendations are from the Parathyroidectomy Guidelines and are very elegant in their logic. This particular chapter was written by Dr. James Lee. I'll show you his picture in a little bit. So patients undergoing parathyroidectomy should have preoperative thyroid evaluation by ultrasound, very sensible, and a strong moderate recommendation with respect to the literature. If there is concomitant primary hyperparathyroidism and thyroid disease requiring resection, thyroidectomy should be done at the time of parathyroidectomy, again, well supported by the literature.

Recommendation three, evaluation for concomitant thyroid disease should follow evidence-based guidelines which, as we know for thyroid, are very available and well done, a strong recommendation and a high level of evidence. And recommendation for the indications for thyroid surgery during parathyroid surgery are the same as for isolated thyroid disease and should follow evidence-based guidelines. In other words, again, a strong recommendation with a high level of evidence.

The problem is that for the rest of this talk is evidence-based guidelines for what to do about parathyroid disease during thyroid surgery. So the AAES Parathyroidectomy Guidelines came out OK. We came in on target for time. We came in on budget. The budget was zero which is remarkable. And so I got to do the next thing for AAES which is thyroidectomy guidelines which was approved by leadership in August of 2016, so just under two years ago.

And they developed thyroidectomy guidelines written by surgeons for surgeons, and we assembled a multi-disciplinary writing group with broad-based expertise in endocrinology, pathology, and surgery. Including Virginia LiVolsi, who's a riot on these conference calls, and Jennifer Sipos of endocrinology and 17 surgeons, including otolaryngologists and six primary authors. The next slide shows everyone's picture. The first author is Dr. Kopal Patel, and Chris McHenry is co-chairing it with me.

Anticipated journal submission is this fall, so we're pretty much on schedule. And this is the group, and here are our six hardworking primary authors, Dr. Yip. This is Carrie Lubitz from MGH. This is Wen Shen from UCSF. Here's Kopal Patel from New York. He's the first author.

There's Barb Miller, and this is Libby Grubbs from M.D. Anderson, and then over here is Electron Kebebew, Ralph Tufano, and Virginia LiVolsi and the rest of the members. This is right at the beginning, when we were all still shiny and smiling, but actually were getting along pretty well, forming a cohesive thing. It's a larger group than last time and a little more disparate in its ability to form consensus, but collegially and pleasantly so, just a lot of different opinions.

The aim of the AAES Thyroidectomy Guidelines is to cohere and exposit best practices in adult thyroid surgery, adults not kids, after decades of change in the field. With consensus recommendations based on the literature, using the American College of Physicians grading scheme and lead for each topic by-- the next slide is the topics-- by a primary author. The subcommittee for each topic has four to eight people on it. And we constructed the subcommittees based on relevant expertise and balancing of author responsibilities with complete lack of topic conflict of interest, which was interesting and challenging. AAES didn't have a COI policy until we started this, and now they do.

The subcommittees formally review the literature to prepare topic outlines and draft text which was then discussed, revised, and re-discussed endlessly to consensus by the entire group. And we're actually going to grade the recommendations in our next couple of meetings. In revision, later this summer and in the fall, we'll be incorporating explicitly-sought AAES member input, plus the obligatory journal peer review, the target journal is *Annals of Surgery* this time, and then, we'll be inviting sister society endorsement, and here are the topics. There are 20 of them, which this slide comes from Kopal Patel, and I thought there were 19. And right now, we're going to talk about the draft recommendations from concurrent parathyroidectomy.

But first a couple of things to keep in mind. The thyroid and the parathyroid glands cohabit. They are two different organs jammed together in the front of the neck. They look alike. They're the same color or similar colors, and they commingled in infiltrated ways, or sometimes one is inside the other. Another point that's important is that the first neck operation is the safest. Initial parathyroid surgery is apples, and reoperation is oranges. They're very differently managed, especially for prepared thyroid, whether it's an initial operation or reoperation right Dr. Mitchell?

Right.

Yes, and parathyroid exploration is different from parathyroid preservation, so let me give a little example of that. It's Christmas, and you're a parent, and you're planning Christmas for the kids, for the family, so you go to the mall for Thanksgiving weekend. And at the mall-- which is a zoo, but the displays are fresh and all shiny-- your goal is to pick up one present for each person in the family. See what else looks interesting, and get home safe and alive. OK? That's parathyroid preservation during thyroidectomy. You have to leave at least one gland behind, typically you want to leave four, but it's got to be at least one. Do no harm, and wave at everything else.

Parathyroid exploration is a different model for Christmas, the real model. You've got to get the tree, the lights, the music, the food, the stockings, the mistletoe. You've got to get that all together, plus you've got the meaning of Christmas. Plus you've got to get a pile of stuff that's about the same value and size, if your kids are young. And you've got to wrap it till one o'clock in the morning, and then you can begin to enjoy the holiday. OK?

That's parathyroid exploration. Sometimes it's easy, and sometimes it's elaborately difficult, but your object in parathyroid expression is to achieve cure, not just wave at the parathyroids. So it's a very different strategy, concomitant thyroid and parathyroid disease can alter, definitely alter, the operative approach. Patients need specific counseling and consents. They can need specific imaging which is on the next slide. You have to schedule PTH monitoring. You have to make sure frozen section is available at your hospital that time of day, et cetera.

So the next three, basically the last three slides, are some draft recommendations about concurrent parathyroidectomy during thyroid surgery from the AAES Thyroidectomy Guidelines. And I don't necessarily agree with these, but the point is consensus, so you'll hear about it. In endocrinology patients with thyroid disease, the rate of concomitant primary hyperpara is 0.2% to 2.5%. But all of these green studies are retrospective, not especially well done, but it's the data we have.

Primary hyperpara in this study was more likely with goiter and with thyroid cancer with nice p-value. In patients who are undergoing thyroidectomy, the rate of biochemical primary hyperparathyroidism is somehow higher, and this is one study. There four or five that have figures around 3% to 5%, so what I think about is 4%. So I'm taking a patient for thyroid surgery. What's the chance that they have hyperpara? 4%. I'm taking a patient for parathyroid surgery. What's the chance that they have thyroid disease? 40%. 4 and 40.

Another 0.9% to 1.9% of patients who have normal calcium and PTH levels actually are found to have a single enlarged parathyroid at surgery. That's actually well-documented in the literature. What to do about it is a little less clear. The text of the draft guidelines says as well that, although the cost effectiveness of parathyroidectomy for primary hyperparathyroidism is well established as opposed to observation. No data on routine preoperative assessment of calcium and PTH yet exist. There's no data on the cost effectiveness of that strategy.

So our program, because we believe in it, routinely measures calcium PTH and vitamin D 25-OH in every thyroidectomy patient preoperatively. We want to know if they have parathyroid disease, and we want to take care of it responsibly, but not all the Thyroidectomy Guidelines authors do that. So based on the literature, the most that we could say, that we could agree on, is that hypercalcemia in a patient scheduled for thyroidectomy should be further evaluated biochemically prior to surgery, and that's a weak recommendation based on low-quality evidence. What does this mean? It's an opportunity to write some papers. OK? Because if there were better evidence, then we'd be able to say something more clear.

We get we call them tinglyers, and we're on call 24/7, unless we're physically out of town. And a tingler phone call at two o'clock in the morning is something that we work very hard to avoid. How do you avoid that phone call? Measure their 25-OH D preoperatively, and if it's low, give them burst therapy preoperatively, which we now use like water. Yeah, because everybody in the Pittsburgh area is vitamin D deficient because of our lack of sunshine and our lack of sunshine. OK.

All right, so this next slide is again text from the draft guidelines. Ultrasound is the preferred initial imaging modality for both disease types. True. In concomitant thyroid disease, parathyroid imaging studies are less sensitive and less specific. True. If there's goiter, it's harder to localize an abnormal parathyroid gland or glands. Further parathyroid imaging can guide exploration, but conversely, it may be unnecessary if you're doing a total thyroidectomy anyway.

There's a lot of dilemma in parathyroid surgery about unilateral exploration guided by PTH minoring versus routine bilateral exploration. If you're going to be over there anyway, do you really need a SPECT-CT? I generally get them, but not in the renal-- anyway, the point is that the chance of a mediastinal gland is about 1 in 1,000, and so from a cost effectiveness standpoint, it may not be necessary to get a SPECT-CT. You asked me about this an hour ago.

From the Parathyroidectomy Guidelines, recommendation 4-4, it talks about parathyroid FNA. And it comes out strong, that it's not recommended, except in unusual difficult cases and certainly not if parathyroid cancer is suspected, but it's based on insufficient evidence. It's basically an opinion. What is the reason for this recommendation? FNA can create histological artifacts that mimic parathyroid cancer under the microscope, and inflammation, the smaller reason, can make surgery much more difficult.

So based on these findings from the prior guidelines, the thyroidectomy authors in their text suggest consulting a surgeon about potential utility prior to proceeding with parathyroid FNA. Now, we do parathyroid FNA sometimes, or do FNA with a PTH wash to see what it is. Because we're concerned that it might otherwise be a malignant nodule, but we talk about it first. The draft guidelines text says, there should be a low threshold for concurrent parathyroidectomy. Yeah. Because it appropriately addresses disease when present, it has risks that are not reportedly higher, and it avoids reoperation which certainly has higher risks and costs.

So the second draft recommendation from the Thyroidectomy Guidelines is when a patient is scheduled for thyroid surgery and is diagnosed with hyperparathyroidism, they should undergo concurrent parathyroidectomy. So you see that it's sensible, it's data-based, strong, recommendation-based on moderate evidence, and it implies that you should check for it anyway. Text also says, there's a higher likelihood of primary hyperparathyroidism in hyperthyroidism in chronic lithium therapy in chronic renal disease, in which case it's secondary, tertiary, and with a family history of MEN 1 or 2a.

And so the third and final recommendation in this chapter of the Thyroidectomy Guidelines is evaluation for primary hyperpara is recommended based on the literature in patients with a family history, because it's strong, moderate. These other things seem sensible, we do them, we recommend it, but there's no literature to support it. So in conclusion, the AAES Thyroidectomy Guidelines aren't done yet. They're still only half baked. And as a member of AAES, we last time took very seriously the constructive comments of members and made substantial changes in some of that text. Plus, then there's the process of journal peer review. This is-- I think I may have said-- planned for submission to *Annals of Surgery*, and then, there's the process of inviting sister society endorsement in the future.

Thank you, and I just put this last slide here to make people laugh. This is a-- I must get this email once or twice a day. Dear Dr. Carty, I've learned that you published an article on hangnail, and the topic has impressed us a lot. The paper has attracted attention from researchers specializing in hangnail. Congratulations. Please submit to us in our open access journal, a new paper, and we'll only charge you 2/3 of the price.

[LAUGHTER]