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Education in the Time of COVID-19

A trainee's perspective

Omar M. El Kawkgi, M.B., B.Ch., B.A.O., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic's campus in Rochester, Minnesota, writes about his perspective as a second-year clinical endocrine fellow: For as long as we can remember as medical trainees, the bulk of learning in our profession happened at the bedside. Indeed, we were residents of the hospital, practically living there just a few years ago. As subspecialty trainees, we learned clinical pearls from seeing patients alongside more experienced clinicians.

In the face of a pandemic, our entire fellowship program switched to a remote approach. We expressed our worries to one another: Will we continue to be exposed to diverse cases crucial to our education? Will my preceptors, previously accessible with a knock on the door, still be available to discuss patient care and, perhaps more importantly, provide me with meaningful feedback to grow from? How will I stay connected to my community of co-fellows whom I normally rely on as my work family?



Omar M. El Kawkgi, M.B., B.Ch., B.A.O.



Kurt A. Kennel, M.D.

In time, we realized we were not alone. We shared, learned and connected with one another through social media. We tweeted back and forth: What is the best videoconference platform for didactic teaching? We received numerous answers and had to try them all until one worked, but we learned. Similarly, we began to learn how the changes created by this situation supplemented our education rather than detracted from it.

Video visits with patients and preceptors meant real-time observation and feedback on our clinical approach. Content sharing technologies meant we could easily but securely share patient data, images and relevant literature. Triaging endocrine problems in the face of a pandemic prompted critical thinking in us. Lastly, it turned out that a weekly check-in virtual meeting — although not the same as a chat in the fellows' room — could still keep us connected and conversing.

All in all, although not a replacement for the traditional bedside learning at the bedside has supplemented our education, and if nothing else, taught us to stay resilient and adaptable.

A program director's perspective

Kurt A. Kennel, M.D., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic's campus in Rochester, Minnesota, reviews his observations as a fellowship program director:

As with all challenges, opportunities await. So I find the Endocrinology Fellowship at Mayo Clinic's campus in Rochester, Minnesota, in the midst of an unprecedented disruption to medical education.

For safety and resource conservation, and due to a pause in nonessential aspects of outpatient practice, most endocrinology fellows worked and learned remotely for the month of April 2020. Management of established patients continued but with clinical scenarios not previously encountered:

Is my elderly patient with osteoporosis at greater risk of infection or fracture if denosumab therapy is delayed in order to stay at home?

A growing list of deferred appointments and new requests thrust fellows into a triage role testing their clinical judgment and, at times, revealing gaps in their knowledge of the course of untreated conditions. Previously a novelty, telehealth — video or phone visits, both inpatient and outpatient — became a staple of practice. Unsurprisingly, the fellows adapted quickly and facilitated the onboarding of faculty to new technology and workflow.

While time to catch up or focus on scholarly pursuits benefited some, the pause in clinical and laboratory-based research required trainees in their research year to adjust their timelines. Similarly, didactic teaching, conferences and journal clubs, and in-the-moment sharing of cases and clinical pearls quickly adapted to virtual meetings, which facilitated engagement of participants outside the institution.

Finally, maintaining the esprit de corps with social distancing required creativity and typically

centered on the sharing of personal rather than professional daily events. Stressful in the best of times, celebration of the transitions from medical training to employment, orientation of the next wave of trainees and selection of new fellows now are done virtually. What do each of us remember about such events that was meaningful when conducted in person?

In hindsight, the uncertainties of the early impact of the pandemic on medical education may pale in comparison with the long-term implications. “There are many things we do during patient encounters that are not that important” was an early observation of a trainee seeing a patient by eConsult in the hospital. Whose perspective does this observation reflect? In contrast, the ability to witness aspects of a patient’s home environment during a video visit provided an aha moment for a trainee previously unaware of barriers to diabetes self-care. The sharing of educational content via digital platforms extended the reach of Mayo Clinic faculty and, hopefully, enticed some residents and student-level attendees to consider a career in endocrinology.

Oncogenic Osteomalacia, Pearls From an Elusive Tumor: A Case From the Endocrine Teaching Clinics

Case

A 36-year-old woman with no significant past medical history presented for evaluation of multiple, nontraumatic fractures discovered during a work-up of diffuse bone pain a year prior to her presentation.

At that time, she had developed progressive bilateral hip pain that was thought to be related to sacroiliitis. She subsequently underwent an extensive rheumatologic work-up that did not identify any inflammatory disorder to explain her symptoms. Radiographic imaging obtained did, however, reveal multiple fractures, including multiple rib fractures, a humeral fracture and sacral fractures. An oncologic work-up that included

multiple bone marrow biopsies did not identify any malignancy.

The patient did not recall any prior fractures. She was healthy as a child and reached expected midparental height during puberty. Neither she nor her first-degree relatives had significant dental issues. Her maternal grandfather developed rickets at age 6, which resolved with appropriate therapy.

Examination did not identify any dental abnormalities or other dysmorphic features. The patient used a wheelchair due to multifocal pain. She underwent various laboratory tests (Table 1).

Computerized tomography (CT) of the chest, abdomen and pelvis revealed a 6-cm cavernous hemangioma of the liver, which the patient had been aware of for at least six years. Technetium-99m (Tc99m) bone scintigraphy (Figure 1) showed increased radiotracer uptake concerning for bilateral sacroiliac insufficiency fractures in addition to posterior left ninth to 12th and right 11th rib fractures. In addition, there were focal areas of uptake in bilateral humeral heads, femoral heads, femurs, tibiae and ankles, all consistent with occult fractures. Whole-body magnetic resonance imaging (MRI), whole-body Tc99m sestamibi scan and a 68Ga-DOTATATE



Natalia Genere, M.D..



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positron emission tomography (PET)-CT did not reveal any evidence of a mesenchymal tumor. *In situ* hybridization studies for fibroblast growth factor 23 (FGF23) were performed on a biopsy specimen obtained from the liver hemangioma and were negative.

The patient was started on calcitriol (1 mcg twice daily) and phosphorus (750 mg three times daily) for medical management of oncogenic osteomalacia. Within eight weeks of initiating medical therapy, she had a significant decline in bone pain, was able to wean off narcotic pain medications and was ambulating freely. At one-year follow-up, serum phosphorus levels were normal and repeat Tc99m bone scintigraphy (Figure 2) showed healing of the previously noted insufficiency fractures. The patient had symptomatically improved but continued to have a high medication burden.

Discussion

Oncogenic osteomalacia — also referred to as tumor-induced osteomalacia (TIO) — is a rare endocrine disorder in which a small bony or soft tissue mesenchymal tumor causes hypophosphatemia via secretion of FGF23. The latter causes hypophosphatemia via two mechanisms: (1) reduction of renal tubular phosphate reabsorption leading to phosphaturia, and (2) impairment of hydroxylation of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D, thus reducing intestinal phosphorus absorption. As a result of chronic hypophosphatemia, patients develop osteomalacia and associated insufficiency fractures.

The diagnosis of TIO should be considered in patients who have musculoskeletal pain with hypophosphatemia, with or without insufficiency fractures. Diagnostic testing should include quantification of the tubular reabsorption of phosphorus, which is reduced in the presence of FGF23; additional diagnostic laboratory and imaging studies are useful for the evaluation of TIO (Table 2). The differential diagnosis of hypophosphatemia includes X-linked hypophosphatemia (consider with younger age of onset, suggestive family history and dental anomalies), proximal renal tubulopathies (consider with multiple electrolyte abnormalities; may be genetic or acquired) and diet-related hypophosphatemia (consider in patients with low intake or refeeding syndrome). An endocrinologist’s perspective of this condition was reviewed in the *Journal of Endocrinological Investigation* in 2018.

When TIO is biochemically confirmed, diagnostic imaging may help identify the

Laboratory test	Result	Reference range
Total serum calcium	9.1	8.8-10.2 mg/dL
Serum phosphorus	2.0	2.5-4.5 mg/dL
Magnesium	2.1	1.7-2.3 mg/dL
Normal kidney and liver functions		
Bicarbonate	24	22-29 mmol/L
Parathyroid hormone (PTH)	40	15-65 pg/mL
25-hydroxyvitamin D	48	20-50 ng/mL
1,25-dihydroxyvitamin D	18	18-78 pg/mL
Total alkaline phosphatase	213	35-104 U/L
Bone-specific alkaline phosphatase	47	< 14 mcg/L in premenopausal women
Serum beta-crosslaps (β-CTX)	478	25-573 pg/mL in premenopausal women
Tubular reabsorption of phosphorus	54.7	> 80%
Fibroblast growth factor 23 (FGF23), C-terminal	139	< 180 RU/mL

Table 1. Patient laboratory testing results.

Test	Considerations
Initial evaluation of hypophosphatemia	
■ Complete electrolyte panel	Presence of multiple electrolyte abnormalities (hypocalcemia, hypokalemia, renal tubular acidosis) may suggest Fanconi syndrome.
■ 25(OH)D and 1,25(OH) ₂ D	If there is a discordance between 25(OH)D and 1,25(OH) ₂ D, this would suggest the presence of an interfering substance (FGF23).
■ PTH	Elevated PTH may result in hypophosphatemia, but this would typically be accompanied by hypercalcemia.
■ Tc99m bone scintigraphy	This may be helpful in patients complaining of diffuse pains as a means of identifying associated fractures.
Confirmation of oncogenic osteomalacia	
■ TRP	Serologic test should be completed while fasting, and second morning void urine concurrently collected. TRP should be high in the setting of hypophosphatemia; a low TRP (< 80%) suggests the presence of a phosphaturic substance (FGF23).
■ FGF23	There are two commercially available tests to measure FGF23: a somewhat less sensitive C-terminal assay and a newer, very sensitive and specific intact FGF23 assay. Elevated FGF23 levels by either method suggest presence of an FGF23 mediated pathologic process such as XLH or oncogenic osteomalacia.
25(OH)D: 25-hydroxyvitamin D; 1,25(OH) ₂ D: 1,25-dihydroxyvitamin D; FGF23: fibroblast growth factor 23; TRP: tubular reabsorption of phosphorus; PTH: parathyroid hormone; XLH: X-linked hypophosphatemia	

Table 2. Testing considerations in oncogenic osteomalacia.

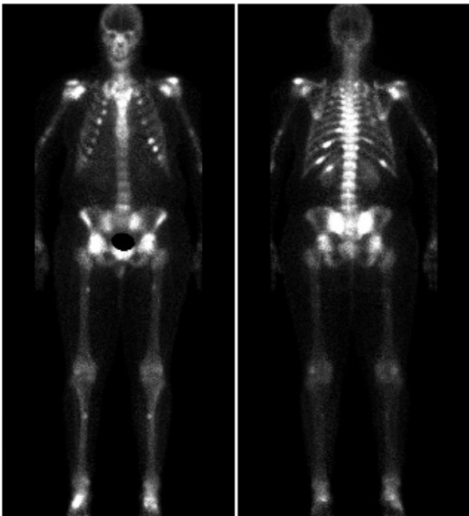


Figure 1. Increased radiotracer uptake of the bilateral sacroiliac region, posterior ninth to 12th ribs on the left, posterior 11th rib on the right, bilateral humeral heads, femoral heads and ankles. Stress fractures of bilateral femurs and tibiae.

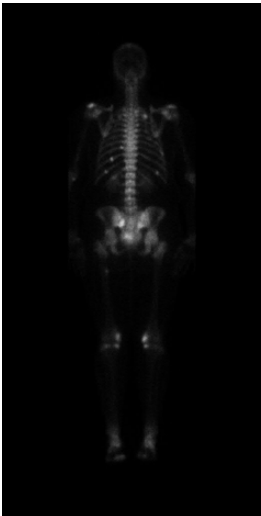


Figure 2. Improvement of multiple fractures involving ribs, sacrum and right proximal femur.

culprit lesion; excision of the tumor can normalize FGF23 levels and reverse the disease process. Functional imaging such as 18F-fluorodeoxyglucose (FDG) PET-CT and octreotide scintigraphy with single-photon emission computerized tomography (SPECT)-CT have been used with some success in identification of these lesions. Anatomical imaging with MRI (whole body or focused on area with positive results on functional imaging) may be considered. Venous sampling for measurement of FGF23 has been used with variable success. While not approved by the Food and Drug Administration (FDA) for mesenchymal tumors, 68Ga-DOTATATE PET-CT was reported in *Clinical Nuclear Medicine* in 2015 to have some success in tumor identification; a current clinical trial (NCT03736564) is investigating its use for this indication.

Tumor identification is commonly unsuccessful early in the disease process; supplementation with phosphorus and calcitriol is the mainstay of medical management. Doses should be escalated, as tolerated, until normalization of serum phosphorus levels. Serial monitoring is necessary because of long-term risks of nephrocalcinosis and secondary hyperparathyroidism, as well as changes in requirements for phosphorus. Imaging studies can be repeated at regular intervals in an effort to identify the culprit lesion and avoid long-term medical management. In June

2020, the FDA approved an FGF23 antibody, burosumab-twza, for the treatment of oncogenic osteomalacia; in addition to improving phosphate metabolism and physical function, this novel therapy may reduce the burden of treatment and monitoring for this difficult condition.

For more information

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Steroid Profiling in the Diagnosis of Malignant Adrenal Masses: Cases From the Endocrine Teaching Clinics

Adrenal masses are found in up to 7% of the population undergoing abdominal imaging, but adrenal tumors larger than 4 cm represent a small proportion of these masses. Adrenocortical carcinoma (ACC) and other malignant adrenal tumors—such as metastases, lymphoma and, rarely, sarcoma—represent 13% and 18%, respectively, of adrenal masses larger than 4 cm evaluated

in endocrine practice, as reported in research published in *Mayo Clinic Proceedings: Innovations, Quality & Outcomes* in 2018.

Tumor size (larger than 4 cm, and particularly larger than 10 cm) as well as unenhanced Hounsfield units (HUs) on computerized tomography (larger than 20 or increased heterogeneity) are strong predictors of malignancy. History of extra-adrenal malignancy is associated with a diagnosis of adrenal metastasis, while a hormonally active adrenal mass (especially combined cortisol and androgen excess) is strongly suggestive of ACC.

Adrenal biopsy is not recommended in any adrenal tumor suspicious for ACC, mostly due to poor accuracy and concern for needle track seeding, as reported in research published in *Clinical Endocrinology* and the *European Journal of Endocrinology* in 2016. Furthermore, adrenal biopsy is an invasive and



Shobana Athimulam, M.B.B.S.



Irina Bancos, M.D.

Steroid profiling, both in serum and in urine samples, is currently clinically available and can provide valuable data to guide appropriate next steps in management, as reported in research published in *Clinical Chemistry* in 2017 and *Endocrine Practice* in 2019. As demonstrated in the following cases, steroid profiling is especially helpful in two clinical scenarios:

- Distinguishing a lipid-poor adenoma from a smaller ACC to decide on laparoscopic versus open adrenalectomy
- Distinguishing ACC from other malignant adrenal masses

A 71-year-old woman was evaluated by her primary care physician for symptoms of worsening shortness of breath. A computerized tomography (CT) scan of the chest did not show any lung pathology but identified an incidental left adrenal mass. Subsequent CT of the abdomen revealed a 15-by-12-cm well-circumscribed heterogeneous left adrenal mass with scattered dystrophic calcifications and marked local mass effect (Figure 1). No other lesions were noted in the abdomen or the chest.

The patient had a known diagnosis of sleep apnea, hypertension, type 2 diabetes mellitus, obesity and dyslipidemia. She reported no personal or family history of any genetic syndrome or malignancy. During evaluation in the adrenal clinic, she was asymptomatic and denied any changes to appetite or weight.

On physical exam, no features of overt Cushing syndrome, acne, hirsutism, androgenic alopecia or edema were noted. Biochemical workup (Table) was consistent with adrenocorticotrophic hormone-independent cortisol excess and androgen excess, without evidence for primary aldosteronism or catecholamine excess. Preoperative serum and urine steroid profiles were consistent with adrenocortical carcinoma, with elevated androgen and glucocorticoid precursors and metabolites (Figure 2). The patient underwent an open left adrenalectomy, and surgical pathology confirmed ACC (Ki-67 index of 70%).

A 65-year-old woman was evaluated for unexplained persistent low-grade fever associated with mild neutrophilia. Her medical history included hypertension, dyslipidemia and prediabetes. In addition, she had a history of stage I uterine



Figure 1. Adrenocortical carcinoma (case 1, arrow) as seen on coronal (left) and transverse (right) views of the computerized tomography of the abdomen.

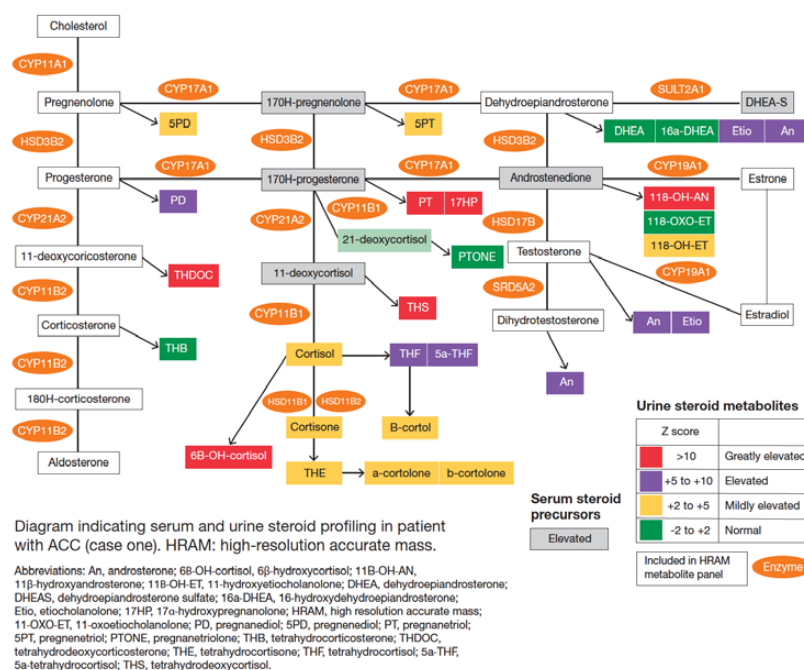


Figure 2. Serum and urine profiling (case 1).

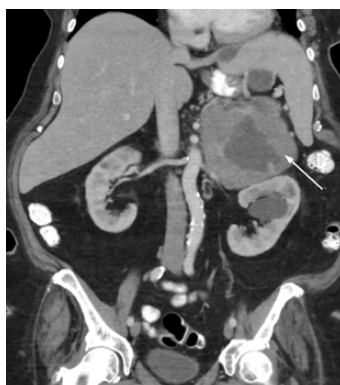


Figure 3. Poorly differentiated leiomyosarcoma (case 2, arrow) as seen on coronal (left) and transverse (right) views of the computerized tomography of the abdomen.

Biochemical Testing	Case 1	Case 2	Reference values
8 a.m. serum cortisol following 1 mg overnight dexamethasone suppression test, µg/dL	16	4.1	< 1.8
ACTH, pg/mL	10	28	7.2-63
DHEA-sulfate, µg/dL	401	54.8	5.3-124
Aldosterone, ng/dL	9.7	6.2	< 21
Plasma renin activity, ng/mL/h	3.8	4.58	2.9-10.8
Plasma metanephrines, nmol/L	< 0.2	< 0.2	< 0.5
Plasma normetanephrines, nmol/L	0.48	0.7	< 0.9
Urine-free cortisol, µg/24h	19	21	3.5-45
Serum steroid profiling			
11-deoxycortisol, ng/dL	3,200	25	10-79
17α-hydroxyprogesterone, ng/dL	N/A	28	< 51
17α-hydroxypregnenolone, ng/dL	64	< 40	31-455
Androstenedione, ng/dL	2,320	N/A	30-200
ACTH: adrenocorticotrophic hormone, DHEA: dehydroepiandrosterone			

Table. Biochemical work-ups of the two patients.

cancer for which she underwent a hysterectomy two years prior to the current evaluation.

The patient had no personal history of genetic syndrome or family history of malignancy. Following an episode of fever with abdominal pain, she underwent a CT of the abdomen that incidentally identified a 20-by-17-by-10.5-cm large mixed solid and cystic mass in the left adrenal gland, with scattered calcifications abutting surrounding structures (Figure 3).

On evaluation in the adrenal clinic, mild hirsutism

was noted without evidence of acne, androgenic alopecia, features of Cushing syndrome or edema. Biochemical work-up (Table) revealed abnormal dexamethasone suppression, but otherwise no hormonal excess. Preoperative serum and urine steroid profiles were not suggestive of ACC. Open left adrenalectomy was performed, and pathology demonstrated a poorly differentiated leiomyosarcoma.

Discussion

These two cases of malignant adrenal tumors are both highly suspicious for ACC based on imaging and standard-of-care hormonal work-up. Serum and urine steroid profiles of the patient in case 1 were highly suggestive of ACC, but those of the patient in case 2 favored other diagnoses, such as metastases or lymphoma. This additional information allowed for individualized approaches to confirm the diagnoses in both patients.

Preoperative diagnosis of ACC will guide a recommendation for open adrenalectomy without delay, as in case 1, whereas excluding

ACC, as in case 2, may lead to reconsideration of adrenalectomy in favor of adrenal biopsy or other diagnostic tests.

Serum and urine steroid profiling should be considered in any patient with an indeterminate adrenal mass (tumor size larger than 4 cm, HUs > 10 and especially HUs > 20) prior to surgery to help guide subsequent diagnostic and therapeutic measures.

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The Steven A. Smith and Lynda D. Smith Family Fund in Diabetes Care and Education: A Parting Gift From Longest-Tenured Leader

Steven A. Smith, M.D., still remembers the day he noticed inconsistencies in the Patient Appointment Guide for patients with diabetes. He discussed it with his colleagues in Endocrinology. It didn't take long for consensus to emerge that the Patient Appointment Guide should be standardized across Mayo Clinic.

The inconsistencies compromised patient safety and pointed to the need for regularly scheduled clinical review of instructions. "When someone realized that it needed to be an institutional effort to develop consistent instructions, who did they call on?" Dr. Smith asks. "The answer is Patient Education, and the results speak

for themselves.” Since 2009, when Patient Education was enlisted to oversee the Patient Appointment Guide, there have been no sentinel events related to patients with diabetes.

Bridging the gap

Clinicians sometimes overestimate patients’ understanding of their health conditions and the actions necessary to adhere to their treatment plans, says Kristin S. Vickers, Ph.D., L.P., research director of Patient Education. Patient education helps bridge that gap between provider assumptions and patient understanding.

“Education is more than information delivery. It’s about clarifying the needs of the learner and the best method for delivering information so that the patient can quickly understand and act on medical expert recommendations,” Dr. Vickers says. “Patient education must be sensitive to numerous learning and behavior change barriers, such as stress and pain. Dr. Smith models for us evidence-based patient education, such that patient health literacy, motivation, understanding of technology, culture and preferences are valued.”

For the last 15 years, Dr. Smith has served as Patient Education’s medical director, advancing its function from Mayo Clinic in Rochester, Minnesota, to all Mayo Clinic locations.

Endowing the future

To ensure Patient Education’s commitment to the science of evidence-based patient education, Dr. Smith has established the Steven A. Smith and Lynda D. Smith Family Fund in Diabetes Care and Education, an endowment to support diabetes research and education. “Diabetes is an up-and-coming, if not already established, epidemic,” Dr. Smith says. “There’s lots of opportunity to help serve individuals in the self-management issue.”

The American Diabetes Association says that 9.4% of Americans have diabetes. Of the 30 million adults with diabetes, 23 million are diagnosed and 7 million are undiagnosed. Diabetes remains the seventh-leading cause of death in the U.S.

“I’m impressed with the exponential growth in patient education science,” Dr. Smith says. “Despite all that is known, challenges remain in getting expert information to the patient at the right time and place. There is promise in the future of the art and science of patient education in the digital age, including the use of technology delivered with a human touch.”

Milestones in patient education

Patient Education dates back to 1976 when the Mayo Clinic Health Learning Center was established in Rochester to instruct patients in self-management of disease and healthy-living habits.



Steven A. Smith, M.D.

In 2009, when it was known as the Section of Patient Education, it began overseeing the Patient Appointment Guide. But standardizing the Patient Appointment Guide is just one of Patient Education’s many milestones.

In 2010, when Patient Education developed the Big 4 Safety Language, instructions for patients with diabetes were the priority. The section name was changed to the Office of Patient Education in 2016 to connect efforts in creating patient education across all Mayo Clinic locations. The Content Convergence Project in 2018 launched delivery of education materials and the Patient Appointment Guide through Epic.

Another milestone, albeit a bittersweet one, was the departure of its longest-tenured medical director. Dr. Smith retired Jan. 20, 2020, after 31 years as a Mayo Clinic endocrinologist. As he enters retirement, Dr. Smith says he knows Patient Education is in good hands. “They made my day every day when I came to work,” Dr. Smith says of staff members in the Office of Patient Education. “They’re very dedicated to the mission of Mayo Clinic. I can’t say enough good things about them.”

Those who have worked with Dr. Smith feel the same way about him. “Because so much of Patient Education work is behind the scenes with the clinical practice to plan, produce and implement patient education, he inspires me in his continual recognition of the expertise of our staff,” Dr. Vickers says. “He has empathy for patients as they struggle to understand complex conditions and work to manage them. Though the phrase ‘patient-centered care’ gets thrown around a lot, he epitomizes this view.”



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Mayo Clinic welcomes inquiries and referrals, and a request to a specific physician is not required to refer a patient.

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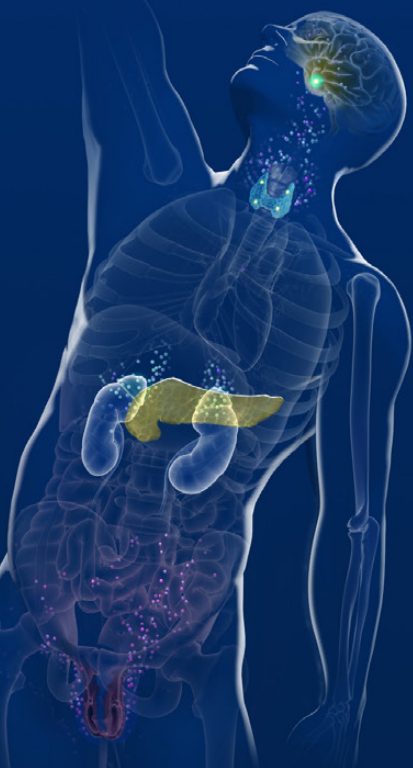
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2020 Graduating Clinical Endocrinology Fellows



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Education Opportunities

For more information or to register, visit <https://ce.mayo.edu/endocrinology>, call 800-323-2688 (toll-free) or email cme@mayo.edu.

Mayo Clinic Thyroid and Parathyroid Disorders Course 2020 — LIVESTREAM

Dec. 5-6, 2020

Topics include a comprehensive review of diagnostic techniques including imaging modalities, molecular testing for evaluation of thyroid nodules, and therapeutic options for management of benign and malignant thyroid and parathyroid conditions.

Endocrine Update 2021 — LIVESTREAM

March 1-5, 2021

This course addresses gaps in medical knowledge to improve patient outcomes. The program covers best practices, barriers to optimal patient outcomes and new approaches to evaluation and management of complex and common endocrine disorders.

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