The Endocrinology Fellowship at Mayo Clinic’s campus in Rochester, Minnesota, is designed to deliver well-rounded clinical and research training. Kurt A. Kennel, M.D., training program director in clinical endocrinology, Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic’s campus in Minnesota, says: “Established in 1969, the program has trained 184 clinicians and scientists to manage and investigate the entire spectrum of endocrine disease. Spanning three years and admitting four trainees a year, the program is one of the largest in the United States. While grounded in training the fundamentals of clinical endocrinology, the curriculum is unique with respect to the breadth and depth of clinical and research training available within one program.”

Keys to the success of the program are:
• The availability and engagement of the 40 subspecialized faculty
• A stimulating academic environment
• A challenging clinical practice

Dr. Kennel explains: “These elements are leveraged throughout a variety of learning formats, each designed to teach the six clinical competencies within endocrinology and to promote scholarship. Rotations in the first year include subspecialty teaching clinics, such as the thyroid nodule clinic, bone clinic and others, where new consultations are used to promote case-based learning and teaching by subspecialty faculty. Weeklong rotations in collaborating departments, such as clinical laboratory medicine, nuclear medicine and endocrine surgery, enhance the fellows’ utilization and interpretation of testing and procedures required for endocrine care. To enhance the fellow’s patient education skills and gain a deeper understanding of the patient’s perspective, the fellows assist with a 2.5-day intensive insulin therapy patient education program for patients and families. Notably, their education in metabolic disorders includes one month of nutrition and bariatric medicine. In addition, endocrine emergencies, perioperative endocrine care and complex inpatient metabolic disorders are managed by a fellow-led inpatient endocrine consulting team with support from advanced practice clinicians who manage the majority of inpatient diabetes consultations. Finally, longitudinal care in a continuity clinic model is used to teach fellows to effectively work within a system of care, to observe the course of disease and the outcomes of management decisions.”

The fellowship leverages the education infrastructure provided by the Mayo School of Graduate Medical Education. Communication and cross-cultural skills are taught in a simulation center using standardized patients. Medical education skills, presentations skills, quality improvement methodology and professionalism are taught by local experts. Within the division, Endocrine Grand Rounds, journal clubs, research seminars and case conferences provide fellows with a daily forum for didactic learning. Training in laboratory research skills, study design and methods, and analysis of resultant data are taught within the laboratory environment. Clinical research coursework taken in the Mayo Graduate School equips fellows to lead clinical research projects with some fellows completing coursework and a thesis to earn a certificate or master’s degree. Workshops on grant writing and writing for publication are offered electively. Ultimately, more educational experiences are offered than can be utilized by a fellow.

Dr. Kennel notes: “Recognizing that each fellow’s goals are different and may change with time, a key feature of the current program is the potential for a flexible third-year curriculum and individualized training to align with the fellow’s interest, ability and career goals. The first year of training includes a uniform curriculum. In the second year, fellows choose a research mentor and dedicate
themselves fully to laboratory-based research, clinical research or a blend of both. Fellows bound for academic medicine and desiring further research training may spend several months of the third year conducting research and working closely with specific faculty for subspecialized clinical training, such as advanced thyroid cancer. Fellows pursuing clinical endocrine practice spend most of their third year acting as a senior fellow in the teaching clinics or hospital service where they supervise and teach internal medicine residents and junior fellows. All fellows in the third year rotate through subspecialty clinics that both consolidate and challenge their knowledge of classic endocrine disease while also extending the spectrum of patients and disorders encountered in fellowship training. Examples of such third-year rotations include transplant endocrinology, pediatric endocrinology and women’s health. Discernment of goals and formulation of a plan to reach them is guided by career and research mentors with whom fellows meet regularly.”

Dr. Kennel concludes: “While the program has been successful, training the next generation of clinicians and scientists will require innovation and refinements to the curriculum based on education research and theory. The recent implementation of accreditation based on educational outcomes, rather than processes, has already spurred new approaches to ensuring that all fellows reach their potential. As a result, applicants seeking excellence in endocrine training should continue to be drawn to Rochester to train in endocrinology.”

Mayo Clinic Endocrinology Fellows 1972 to Present
A 51-year-old woman was referred to Mayo Clinic for evaluation of persistent hypercalcemia after parathyroid surgery. She was diagnosed with primary hyperparathyroidism at an outside institution one year prior with appropriate laboratory work-up, including elevated 24-hour urine calcium excretion, and deemed a suitable candidate for surgery given persistent fatigue and osteopenia documented with bone mineral density testing.

Preoperative imaging, including neck ultrasound and a parathyroid sestamibi scan, failed to localize abnormal parathyroid tissue. She subsequently underwent bilateral neck exploration with left superior, left inferior and right inferior parathyroidectomy as well as right superior parathyroidectomy with auto-transplantation into the left neck infrahyoid muscles.

The patient’s serum parathyroid hormone (PTH) levels were persistently elevated intraoperatively and, unfortunately, she continued to have biochemical primary hyperparathyroidism postoperatively. Additional imaging included a neck ultrasound, parathyroid sestamibi scan and 4-D computerized tomography (CT) neck scan — all of these imaging modalities
failed to localize a parathyroid adenoma.

The patient’s past medical history was significant for depression and primary hypothyroidism. There was no family history of hypercalcemia or parathyroid surgery. Relevant medications included cholecalciferol 10,000 IU once daily.

Her laboratory evaluation at Mayo Clinic was consistent with persistent primary hyperparathyroidism (Figure 1). Parathyroid sestamibi imaging with single-photon emission computerized tomography (SPECT) showed ectopic sestamibi uptake in the lower right midchest without discordance in the neck on planar images. SPECT images confirmed an approximately 1-cm soft tissue nodule in the right paracardiac fat superiorly and just anterior and to the right of the lower superior vena cava and above the right atrial junction, consistent with a solitary parathyroid gland in the anterior mediastinum (Figures 2A and 2B). Arterial phase magnetic resonance imaging of the chest confirmed an enhancing 7-mm nodule in the right lobe of the residual thymus in the anterior mediastinum (Figure 3), corresponding to the focal sestamibi uptake on SPECT imaging.

Endocrine and Thoracic Surgery collaborated to perform a partial thymectomy and resection of intrathymic ectopic parathyroid gland through right thoracoscopy and parathyroid auto-transplantation to the right superior chest wall. Intraoperative serum PTH concentrations dropped to < 6 pg/mL. Surgical pathology revealed an intrathymic parathyroid adenoma (30 mg) with hypercellular parathyroid tissue. The patient recovered well and had a resolution of her hypercalcemia postoperatively.

In the re-operative setting in particular, surgery can be challenging due to anatomical variability, limited localization studies and the possibility of supernumerary glands; therefore, a good understanding of the anatomy and embryology of the parathyroid glands is important to minimize the risk of permanent hypoparathyroidism.

Accurate localizing imaging studies including a neck ultrasound, parathyroid sestamibi scan and MRI are essential. In this patient, the imaging studies performed before the patient’s first surgery failed to show the culprit lesion because the region of interest scanned did not extend inferiorly enough to sufficiently assess the mediastinum. Parathyroid sestamibi imaging with SPECT can improve the sensitivity in localizing parathyroid adenomas and increase diagnostic confidence. Intraoperative ultrasound and PTH sampling are important to ensure that the culprit lesion has been successfully resected.

**Key message**

Ectopic parathyroid tissue should be considered in patients with persistent primary hyperparathyroidism, and when this occurs, surgical management is best undertaken by a multidisciplinary team.

### Blood test

<table>
<thead>
<tr>
<th>Blood test</th>
<th>Result</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium, mg/dL</td>
<td>10.6</td>
<td>8.9-10.1</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>2.8</td>
<td>2.5-4.5</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
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<td>0.6-1.1</td>
</tr>
<tr>
<td>Parathyroid hormone, pg/mL</td>
<td>114</td>
<td>15-65</td>
</tr>
<tr>
<td>Total 25-hydroxyvitamin D, ng/mL</td>
<td>82</td>
<td>20-50</td>
</tr>
</tbody>
</table>

**Figure 1.** Laboratory values obtained after the first operation, but before the second operation.

**Figure 3.** Arterial phase magnetic resonance imaging of the chest confirmed an enhancing 7-mm nodule (arrow) in the right lobe of the residual thymus in the anterior mediastinum.

**Figures 2A and 2B.** Axial (A) and coronal (B) images from parathyroid sestamibi SPECT scan demonstrating right paracardiac soft tissue nodule with intense sestamibi uptake (arrows).
Preventing Type 2 Diabetes Mellitus: Insights From Genetic Studies

Diabetes mellitus in the U.S. causes morbidity and mortality and costs in excess of approximately $170 billion a year. Therefore, identifying ways to prevent diabetes is important. Adrian Vella, M.D., Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic in Rochester, Minnesota, says: “The states of impaired fasting glucose and impaired glucose tolerance are associated with a high rate of progression to type 2 diabetes mellitus. However, the risk is heterogeneous. For example, in Olmsted County, Minnesota, 40 percent of people with a fasting glucose ≥ 110 mg/dL progress to overt diabetes within a 10-year period, as opposed to 5 percent of those with a fasting glucose < 95 mg/dL. While environmental factors and obesity play a role in progression from prediabetes to diabetes, genetic factors are indubitably important. To date there are approximately 65 common genetic variants reproducibly associated with type 2 diabetes mellitus. However, the greatest risk is associated with variation in the gene TCF7L2. The effect size is significant; for example, in the Diabetes Prevention Program, the TT genotype of TCF7L2 at rs7903146 conferred a 2.41-fold increase in risk of type 2 diabetes mellitus compared with the CC genotype. Given the frequency of the diabetes-associated allele — T — of between 30 and 35 percent in most populations and its effect size, this variant makes a substantial contribution to type 2 diabetes mellitus predisposition in a population.”

Type 2 diabetes mellitus is characterized by defects in insulin secretion and action, with impaired postprandial suppression of glucagon. Dr. Vella highlights: “It has been reported that diabetes-associated variation in TCF7L2 impairs post-challenge insulin concentrations in most studies. We hypothesized that the diabetes-associated allele in this locus (rs7903146) impairs insulin secretion, and this defect would be exacerbated by acute free fatty acid (FFA)-induced insulin resistance. We studied 120 individuals, 60 homozygous for the diabetes-associated allele (TT) at rs7903146 and the remainder homozygous for the protective allele (CC). Using methods independent of insulin concentrations (which reflect both insulin secretion and hepatic extraction of insulin), we have confirmed that subjects who are free of diabetes with the T allele have decreased β-cell responsivity (ϕ) for a given degree of insulin action (S) — the hyperbolic relationship between insulin action and β-cell responsivity is shifted to the left in the TT subjects (Figure 1).”

Dr. Vella continues: “More importantly, diabetes-associated variation in TCF7L2 impairs postprandial suppression of glucagon secretion — an aspect of islet function that has been ignored in prior genotype-phenotype correlation studies. This is independent of β-cell function and exacerbated by acute insulin resistance — in this case by raising circulating FFA concentrations (Figure 2). The contribution of α-cell function (if any) to the progression to diabetes is not known. However, if hyperglucagonemia, alone or in combination with a defect in insulin secretion predisposes to diabetes, this would have significant implications for the prevention of type 2 diabetes mellitus.”

![Figure 1. The hyperbolic relationship of β-cell responsivity (ϕ) and insulin action (S) in subjects with the TT genotype at rs7903146. Based on Diabetes. 2016;65:371.](image1)

![Figure 2. Glucagon in response to a 1g/kg body weight glucose challenge with accompanying infusion of intralipid and heparin in subjects with CC (open circles) and TT (solid circles) genotype. Values plotted are means ± SEMs *P < 0.05 for a post hoc unpaired, two-tailed test. Based on Diabetes. 2016;65:371.](image2)
Education Opportunities

16th Annual Nutrition and Wellness in Health and Disease 2016
Sept. 30-Oct. 1, 2016, at InterContinental Chicago, Chicago

Nutrition, physical activity and other healthy lifestyle behaviors are vital components in the promotion of health and the treatment of disease. This course — designed for physicians, advanced practice clinicians, dietitians, nurses, and health and wellness staff — provides a full-spectrum, in-depth overview of situations and topics that clinicians encounter in the ambulatory setting, including obesity in adults and children, individual and group-based weight management strategies, prevention of common medical conditions through healthy lifestyles, nutrition topics in the news, behavior modification, and resilience, plus physical activity and wellness focus for attendees and their patients. A culinary demonstration highlights techniques to prepare healthy, great-tasting food. Presentations offer practical clinical management pearls, interactive case studies and panel discussions. For more information, visit https://ce.mayo.edu/nutrition/content/16th-annual-nutrition-and-wellness-health-and-disease-2016 or call 800-323-2688 (toll-free). Course hashtag: #MayoNutrCME

20th Annual Mayo Clinic Endocrine Update 2017
Jan. 30-Feb. 3, 2017, at The Ritz-Carlton, South Beach, Miami Beach, Fla.

Designed for endocrinologists and interested internists and surgeons, this course addresses gaps in medical knowledge and barriers in clinical practice to improve the outcomes of patients with endocrine and metabolic disorders. Topics span the full range of endocrinology through lectures, debates, panel discussions, clinicopathologic sessions, clinical pearls sessions, informal breakfast roundtable discussions and small-group discussions with experts. Attendees have plenty of opportunity for interaction with the course faculty, who are selected for their expertise and clinical acumen. For more information, visit https://ce.mayo.edu/endocrinology/content/20th-annual-mayo-clinic-endocrine-update-2017 or call 800-323-2688 (toll-free).

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Endocrinology Update

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2016 Graduating Endocrine Fellows
2016 Graduating Endocrine Surgery fellow Zahraa AlHilli, M.B., B.Ch., BAO, Cleveland Clinic, Cleveland, Ohio; and Melanie L. Richards, M.D., program director, Endocrine Surgery Fellowship.

2016 Graduating Endocrine fellows Spyridoula Maraka, M.D., Division of Endocrinology, University of Arkansas for Medical Sciences and Central Arkansas Veterans Healthcare System, Little Rock, Arkansas; Naykky M. Singh Ospina, M.D., University of Florida, Gainesville, Florida; Kurt A. Kennel, M.D., program director, Endocrinology Fellowship, Mayo Clinic, Rochester, Minnesota; and Ana E. Espinosa de Ycaya, M.D., University of Panama, Panama City, Panama.