MAYO CLINIC

EndocrinologyUpdate

Endocrinology News From Mayo Clinic

Vol. 16, No.1, 2021

INSIDE THIS ISSUE

Mayo Clinic Healthy Living Program for Optimization of Bone Health

As people age, their risk of fracture, often resulting from a fall, increases. "Falls and especially fractures can lead to functional decline, impacting the ability to live independently and pursue activities and interests," says Kurt A. Kennel, M.D., Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic in Rochester, Minnesota. "This outcome is especially true for people living with osteopenia or osteoporosis, particularly those with frailty or sarcopenia. But what can people do about it?

"In addition to ensuring safety in home and living environments, they can improve functional fitness and bone strength through exercise. But is it safe to exercise with low bone mass? Done correctly, yes. Can one become more active at an older age? Of course. Can one develop activities that are compatible with their own limitations? Yes, they can."

Dr. Kennel discussed the exercise options available with Alynn C. Dukart, P.T., D.P.T., Mayo Clinic Healthy Living Program, at Mayo Clinic in Rochester, Minnesota, who supplied the following information about the center's Healthy Living Program and its approach to improving bone health.

Motto of the Mayo Clinic Healthy Living Program

- **Safe movement:** Instruction in proper lifting and body mechanics and individualized spine and hip precautions
- **More movement:** Realistic tips and education for decreasing sedentary time and increasing overall activity throughout the day
- **Effective movement:** Education and a personalized program regarding weight-bearing exercise, strength training and balance

Mayo Clinic Healthy Living Program offers a group class that provides general education on exercise and bone density, as well as private sessions with a physical therapist or dietitian. The main goal of the private sessions with a physical therapist is to help an individual establish an effective and safe exercise program that is specifically tailored to bone health.

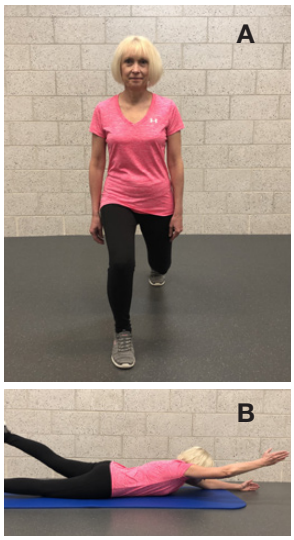


Figure 1. A. Lunge loading the hips and spine. B. Prone spinal extension loading the spine.

While there is evidence in support of weight-bearing exercise, strength training and spinal extension exercises for maintaining and slightly improving bone density, there are many exercise principles that need to be taken into consideration to ensure optimal program effectiveness. It is also prudent to individualize the program based on each patient's skill level and other medical history to ensure proper technique, safety, and ultimately, compliance and effectiveness. For example, two women of the same age with identical T-scores might need to have significantly different programs depending on their exercise experience, body awareness, strength, mobility and balance.

The exercise principles that apply to patients with osteoporosis include

Kurt A. Kennel, M.D.

Alynn C. Dukart, P.T., D.P.T.

exercise specificity, volume, overload and progression.

Exercise specificity

Impact and weight-bearing exercises

Ideally, these exercises should have an impact and load component that includes bearing weight or impact into the ground. Each time the foot strikes the ground, or steps or lands on a surface, that impact helps signal and stimulate bone metabolism. Consider lunges, step-ups or hopping.

Site-specific exercises

These exercises must put a physical loading pressure on the areas of concern. For example, to improve bone density in the hips and spine, load the hips and spine (Figure 1).

Multijoint involvement

The more joints that are involved, the more muscle groups that are mobilized and strengthened. A seated leg extension machine only works one joint (the knee) and one muscle (the quadriceps) as opposed to a standing lunge that works mobility in three joints (the hip, knee and ankle), strengthens multiple muscle groups (glutes, quadriceps, hamstrings, calves and lateral hip musculature), and stretches the hip flexor and quadriceps of the hind leg.

Multidirectional loading

Bone responds better to multidirectional loading, so it's important to exercise and load bones in multiple directions and planes of motion (Figure 2).

Function

Which is more functional, a seated knee extension exercise or a lunge? In everyday life, what motions do people do that are similar to a seated knee extension? Not many, if at all. A lunge, however, replicates many important daily activities, including getting up and down off the floor. Similarly, every time you get up and down from a chair or toilet you are performing a squat.

Safety

When patients are told to not bend forward or flex their spines to pick up something to reduce fracture risk, it is important that they learn instead the proper technique to lift objects by performing a full squat or lunge properly and safely.

Volume

For any exercise, three to five sets of six to 12 repetitions (for a total of about 30 to 36 repetitions) is deemed most effective.

Figure 2. Examples of multidirectional exercises. A. Lunge clocks (12 o'clock, 3 , 3 o'clock and 6 o'clock). B. Side step-ups. C. Hopping in various directions.

Overload

Load and intensity need to exceed that of daily activities to provide benefit.

Walking

Research shows that to achieve benefit on bone mineral density, intensity during walking should aim to exceed 80% of maximal heart rate. Faster speed equates to greater ground reaction force, which helps stimulate bone remodeling. Recent studies have suggested that interval training is more effective than steady state walking or running. At the Mayo Clinic Healthy Living Program, some patients opt for a stress test to ensure accurate heart rate zone recommendations and sufficient safety for their programs.

Progression

To build on the beneficial results of the exercise program, the stimulus must be progressively increased; otherwise, the body does not perceive any overload, which can result in a plateau. Each individualized program should be revisited every two to three months (Figure 3).

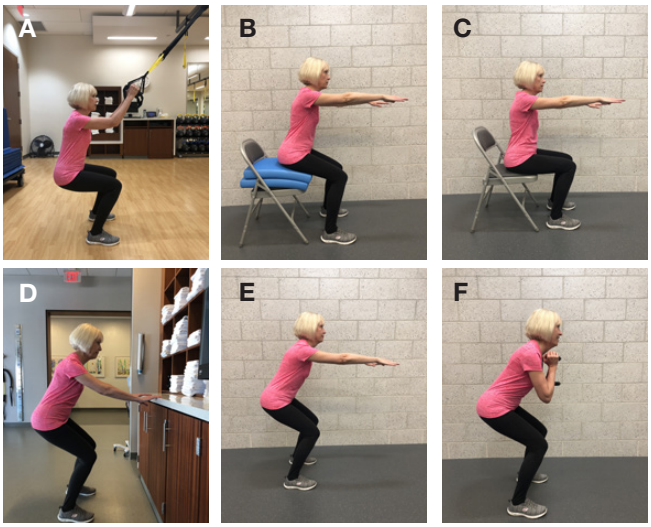


Figure 3. Examples of progressive exercises. A. Assisted squat or lunge via a suspension apparatus in which body weight is offloaded. B. Sit to stand from chair with cushions or pillow. C. Sit to stand from chair. D. Mini counter squats. E. Body-weight squat or lunge working toward full range of motion. F. Slow addition of weight and progression to squat and lunge variations once full range of motion is achieved.

Spinal and hip precautions

Spinal flexion is the highest-risk movement for fracture, in addition to spinal rotation or side bending, and especially combination movements. However, the specific precautions may vary per individual due to individual differences in spinal and hip range of motion, body awareness, other medical conditions and overall strength, as well as the T-score and perhaps even trabecular bone score (TBS). For example, a 50-year-old woman with a spinal T-score of -1.5 and a good TBS who has excellent spinal range of motion, body awareness, fitness level and strength may not need spinal precautions as strict as those for an 80-year-old woman with a T-score of -2.8, poor TBS, and poor body awareness and mobility.

Other considerations

Other factors to consider when planning an exercise program for bone density include patient uncertainty, the benefits of Pilates and yoga, and proper lifting and weight restrictions.

Fear of the unknown

Most patients with osteoporosis or osteopenia want to do whatever they can to improve or maintain their bone density, but unfortunately most don't know where to start and are also confused about what they should and should not do. This uncertainty results in many of them avoiding exercise or limiting themselves in terms of intensity or load.

Pilates and yoga

While Pilates and yoga do contain movements or postures with spinal flexion, rotation, side bending, and hip external and internal rotation, there are many beneficial aspects, too, especially for spinal extension and balance. Prone spinal extension exercises are very beneficial for bone density, and balance is important for fall risk reduction.

Lifting and weight restrictions

It is common for patients to be told to not lift more than 10 pounds, to avoid flexing their spines while lifting. However, the reality is that no one should bend forward to lift an object with a rounded spine regardless of the weight, since it is not ideal body mechanics.

Conversely, it is important to distinguish between bending forward to lift an object and lifting weights as part of a strength training program. Patients should understand that strength training is beneficial and many strength training exercises can safely be completed with more than 10 pounds of weights.

There are many factors at play when developing a bone density exercise program. Other than the overarching guiding principles, there is really no one-size-fits-all program: Some exercises may be safe for one person but not be safe for another, and while a 10-pound squat might optimally load someone, it might not optimally load someone else. In addition, if someone has any other medical conditions or joint pain, modifications may be needed to address those areas of concern.

For more information

Mayo Clinic Healthy Living Program. *https://healthyliving.mayoclinic.org/*. Mayo Clinic.

Mayo Clinic Healthy Living Program for optimization of bone health. *https://www.mayoclinic.org/medical-professionals/endocrinology/videos/mayo-clinic-healthy-living-program-for-optimization-of-bone-health/vid-20484529*. Mayo Clinic.

Advanced Weight Management Program at Mayo Clinic Uses Telemedicine To Expand Services and Improve Patient Outcomes

Manpreet S. Mundi, M.D.

Julia A. Jurgensen, APRN, C.N.P., D.N.P.

Obesity is a life-limiting disorder associated with a number of comorbidities. Currently more than two-thirds of U.S. adults are overweight (body mass index 25 kg/m^2 or higher) and over one-third are obese (BMI ≥ 30 kg/m^2 or higher).

"If current trends hold," expands Manpreet S. Mundi, M.D., Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic in Rochester, Minnesota, "the overall prevalence of obesity in the U.S. is expected to rise to close to 50% by 2030, with 29 states having higher than 50% prevalence." Similar trends are expected worldwide, where 500 million adults are obese currently. This number is estimated to increase to 1.12 billion by 2030.

Dr. Mundi notes: "Management of obesity can be challenging. It needs to be considered from many different perspectives, given multifactorial etiology. There is not a one-size-fits-all answer to weight loss, and maintenance often requires ongoing care. Additionally, with expected rise in prevalence over the next decade, many current models are unsustainable, requiring us to continue to evolve and adapt to meet the needs of this ever-growing population.

"In considering these factors, the advanced weight management program team evaluated the current state of obesity practice and noted that extensive resources were expended on patients with low or minimal motivation or comorbidities. Due to this factor, we decided to expand the program to begin prior to the patient arriving in Rochester."

In December 2018, a nurse triage phone call was implemented to assist program providers to better serve individual patients once they arrive on campus. "This triage call provides a foundation of medical history and understanding of patient needs as well as concerns related to obesity," says Dr. Mundi. Information gathered in the phone call is reviewed by one of the program's nurse practitioners to determine the patient's candidacy, as well as which pathway the patient should be started on when arriving on campus. The advanced weight management program currently offers four pathways to weight loss: lifestyle, weight-loss medication, endoscopic procedures and bariatric surgery.

Julia A. Jurgensen, APRN, C.N.P., D.N.P., Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic in Rochester, Minnesota, adds, "The weight management nurses have developed an excellent approach to these phone calls that allows me and colleagues to best understand the needs of the patient prior to the patient's arrival on campus."

Patients are also directed to review the Weight Management page on Mayo Clinic Connect prior to their visit to learn more about each of the weight-loss pathways offered. The page is updated several times each month by Mayo Clinic weight management experts offering advice and discussion about the most recent developments in weight-loss options. The page allows patients to remain engaged by reviewing the weight-loss options in depth before their initial visit.

"Once the patient arrives on campus, our goal is to meet their needs efficiently, through a tailored itinerary with a team-based approach involving physicians, psychologists, nurse practitioners, physician assistants, nurses and dietitians with expertise in obesity management," says Dr. Mundi. "Depending on the patient's needs and pathway choice, additional visits may be necessary. Video technology has allowed some of these visits to be conducted from the patient's home."

Jurgensen notes: "The feedback has been overwhelmingly positive for these additional video visits, as they allow patients from around the country to follow up with the medical team after weight-loss procedures. That follow-up is critical to their success."

For more information

Mayo Clinic Connect. Weight Management. *https://connect.mayoclinic.org/page/weight-management-1/.* Mayo Clinic.

A Nonadenoma Pituitary Mass: A Case From the Endocrine Teaching Clinics

A 44-year-old man with no significant past medical history presented with fatigue and a newly discovered 1.8 cm pituitary mass. He reported a six-month history of progressive fatigue and over the last two months had developed orthostatic hypotension, erectile dysfunction, polyuria and polydipsia. Along with these signs and symptoms, he noted weight loss of 18 pounds, loss of appetite and fever. The patient also experienced rhinorrhea with clear, water-like nasal secretions that did not respond to nasal steroids for the last three weeks. On exam, he appeared ill and fatigued. Visual field testing confirmed a bitemporal superior quadrantanopsia (Figure 1).

Findings on laboratory studies were consistent with panhypopituitarism (Table).

A water deprivation test confirmed central diabetes insipidus. Pituitary-directed head magnetic resonance imaging (MRI) revealed a 1.8 cm soft tissue mass in the sella extending into the suprasellar cistern with distortion of the optic chiasm (Figure 2, page 6). The mass appeared heterogeneous with low attenuation in neighboring tissue and thickening of the sphenoid air cells.

The patient received transsphenoidal resection of the pituitary mass. Grossly, the inner portions of the pituitary mass appeared milky and necrotic, concerning for a pituitary abscess. His pathology showed acute and chronic inflammation with no evidence of immunoglobulin G4 or lymphoproliferative disease. No organisms were noted microscopically, and bacterial and viral cultures of the pituitary material had no growth. An extensive infectious disease work-up was completed with normal results.

The patient was treated empirically with a course of ertapenem. Three months later, he developed worsening headache, fever, chills and visual changes. MRI showed the pituitary mass extending into the sphenoid and cavernous sinuses (Figure 3, page 6). A pituitary biopsy was inconclusive. Eventually, culture of his cerebrospinal fluid grew Nocardia farcinica approximately one month after collection.

The patient completed a course of targeted antibiotic therapy with trimethoprim-sulfamethoxazole and linezolid with lasting resolution of his symptoms. MRI showed shrinkage of the pituitary mass (Figure 4, page 6).

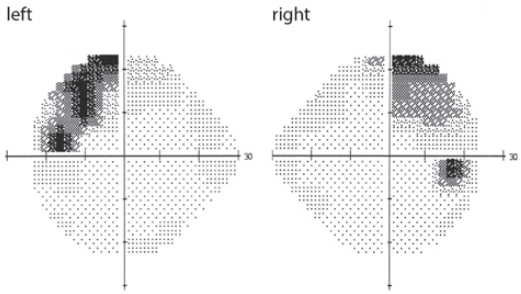


Figure 1. Visual field testing confirming bitemporal superior quadrantanopsia.

Lucinda M. Gruber, M.D.

William F. Young Jr., M.D.

Laboratory Testing Results

Blood tests	Result	Reference range
TSH	0.3	0.3-4.2 mIU/L
Free T4	1.0	0.9-1.7 ng/dL
Prolactin	14	4-15.2 ng/mL
Luteinizing hormone	1.6	1.3-9.6 IU/L
Total testosterone	< 7.0	240-950 ng/dL
Bioavailable testosterone	< 0.6	61-213 ng/dL
Morning cortisol	1.9	7-25 mcg/dL
ACTH	13	7.2-63 pg/mL
IGF-1	48	44-275 ng/mL
White blood cells	5.5	3.4-9.6 x10⁹/L
Neutrophils	2.61	1.56-6.45 x10⁹/L
Lymphocytes	1.89	0.95-3.07 x10⁹/L
Erythrocyte sedimentation rate	26	< 22 mm/h
C-reactive protein	9	< 8 mg/dL
Angiotensin-converting enzyme	21	8-53 U/L
Myeloperoxidase antibody	< 0.2	< 0.4 U
Proteinase 3 antibody	< 0.2	< 0.4 U

Table. Findings on laboratory studies were consistent with panhypopituitarism.

Discussion

Pituitary adenomas account for the majority of sellar masses. Our case highlights the challenges of diagnosis when a patient presents with a more unusual pathology.

Clinical findings suggestive of a nonadenoma pituitary mass include:

- Rapid onset of symptoms (for example, over weeks)
- Constitutional signs and symptoms (fever, chills, weight loss)

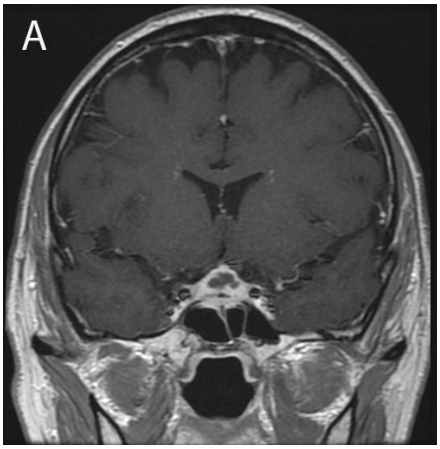


Figure 2. Initial presentation: 1.8 cm soft tissue sellar mass on MRI.

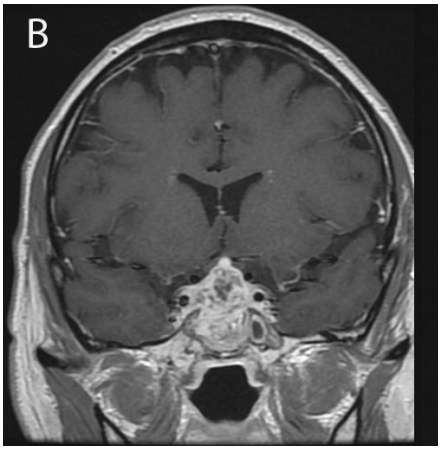


Figure 3. Three months after initial presentation: Enlarging sellar mass with extension into the sphenoid and cavernous sinuses on MRI.

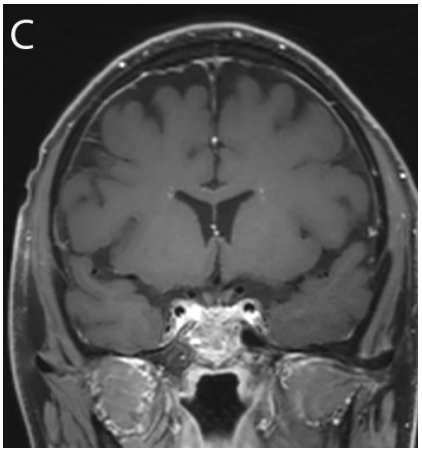


Figure 4. Post-treatment with targeted antibiotic therapy: Improvement in the size of the sellar mass as shown on MRI.

- Neurological symptoms
- New rhinorrhea, concerning for cerebrospinal fluid leak
- Presence of diabetes insipidus
- Elevated inflammatory markers
- Pituitary mass with peripheral enhancement on magnetic resonance imaging

These are signs and symptoms that suggest a sellar mass may not be a pituitary adenoma. The differential diagnosis includes infectious, inflammatory and neoplastic processes. An extensive laboratory and pathology evaluation may be necessary to confirm the diagnosis.

Pituitary abscess is a rare finding. As noted in research published by Agyei and others in *World Neurosurgery* in 2017, patients often present with headache and visual symptoms rather than fever. Staphylococcus organisms are the most common cause, but fungal infections also can occur. However, culture testing is often negative, as in this case, and empirical antibiotic therapy is needed. Imaging findings are often similar to those of pituitary adenomas, but intraoperative findings show purulent material and no evidence of other pathology.

As reported in research published by Carpinteri and others in *Best Practice and Research Clinical Endocrinology and Metabolism* in 2009 and Esposito and others in *Pituitary* in 2017, inflammatory and granulomatous processes such as sarcoidosis or vasculitis can also present as pituitary masses and pituitary dysfunction, often including diabetes insipidus. Langerhans cell histiocytosis and Erdheim-Chester disease can have a similar presentation. The majority of these inflammatory processes also cause systemic symptoms at the time of presentation. A neoplastic process also can occur in the sella, such as lymphoma or germ cell tumors. Primary pituitary carcinomas are very rare, as supported by research published by Pernicone and others in *Cancer* in 1997.

A sellar mass is typically a pituitary adenoma, but rarer diagnoses, such as pituitary abscess, sarcoidosis, vasculitis or lymphoma, should be considered when a patient presents with rapid onset and progression of symptoms, diabetes insipidus, or a heterogeneous pituitary lesion on imaging.

For more information

Agyei JO, et al. Case report of a primary pituitary abscess and systematic literature review of pituitary abscess with a focus on patient outcomes. *World Neurosurgery.* 2017;101:76.

Carpinteri R, et al. Pituitary tumours: Inflammatory and granulomatous expansive lesions of the pituitary. *Best Practice and Research Clinical Endocrinology and Metabolism.* 2009;23:639.

Esposito D, et al. Pituitary dysfunction in granulomatosis with polyangiitis. *Pituitary*. 2017;20:594.

Pernicone PJ, et al. Pituitary carcinoma: A clinicopathologic study of 15 cases. *Cancer*. 1997;79:804.

Select Thyroid Clinical Trials at Mayo Clinic

Therapy of small papillary thyroid carcinoma with radiofrequency ablation

Mayo Clinic investigators are conducting a therapeutic pilot study for small papillary thyroid carcinomas that measure up to 1.5 cm in maximum diameter. The study involves the use of radiofrequency ablation to treat this type of cancer if its position within the thyroid is favorable for this procedure.

Patients will be included if they have no evidence of multifocality, lymph node involvement or distant disease, and if they would be considered otherwise good candidates for active surveillance or ethanol ablation.

The procedure, which requires general anesthesia, will be performed in Radiology at Mayo Clinic in Rochester, Minnesota. Safety monitoring will be conducted via face-to-face visits as well as phone calls during the first month following the procedure. Evaluations for efficacy will occur at Mayo Clinic in Rochester, Minnesota, at three, nine and 18 months from the date of the procedure.

This approach is based on the Mayo Clinic's experience with radiofrequency ablation for benign thyroid nodules, which has led to excellent patient outcomes in the past six years.

Interested patients or referring providers can contact Marius N. Stan, M.D., principal investigator, Endocrinology, Diabetes, Metabolism, and Nutrition, at Mayo Clinic in Rochester, Minnesota, at *Stan.Marius@mayo.edu*.

For more information

Clinical trials: A Study to Evaluate Treatment of Papillary Thyroid Carcinoma With Radiofrequency Ablation. Mayo Clinic.

Therapy for active and moderately severe thyroid eye disease

Mayo Clinic investigators are currently conducting a placebo-controlled interventional trial testing a new therapy for patients with thyroid eye disease (TED), also known as Graves' ophthalmopathy or Graves' orbitopathy (GO).

This phase II study enrolls patients that have active TED or GO with a clinical activity score of 4 or higher and of moderate severity, and in whom the onset of the disease occurred within the past nine months. Patients will be randomized on a 3-1 ratio to receive either a placebo or an anti-neonatal Fc receptor (FcRn) monoclonal antibody with the goal of decreasing thyrotropin receptor antibody levels by 70% to 80%.

Enrolled patients will be evaluated jointly by Mayo Clinic experts in Endocrinology and Ophthalmology. The primary outcome is improvement in proptosis by at least 2 mm at the end of the intervention phase. The intervention will be administered weekly for 12 weeks as a subcutaneous injection at the Clinical Trials Unit at Mayo Clinic in Rochester, Minnesota. Subjects' travel and lodging costs may be covered by the study sponsor.

This novel approach to the treatment of TED or GO is based on the very encouraging safety results from the phase I clinical trial as well as positive efficacy results of the phase II clinical trial in patients with myasthenia gravis.

Interested patients or referring providers can contact Marius N. Stan, M.D., principal investigator, at *Stan.Marius@mayo.edu*, or Jane G. McGlinch, research study coordinator, at *McGlinch.Jane@mayo.edu*.

For more information

Clinical trials: A Study to Evaluate RVT-1401 for the Treatment of Patients With Active, Moderate-to-Severe Graves' Ophthalmopathy. Mayo Clinic.

Marius N. Stan, M.D.

Mayo Clinic
Endocrinology Update

Endocrinology Update is written for physicians and should be relied upon for medical education purposes only. It does not provide a complete overview of the topics covered and should not replace the independent judgment of a physician about the appropriateness or risks of a procedure for a given patient.

Contact Us

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

Phoenix/Scottsdale, Arizona
866-629-6362

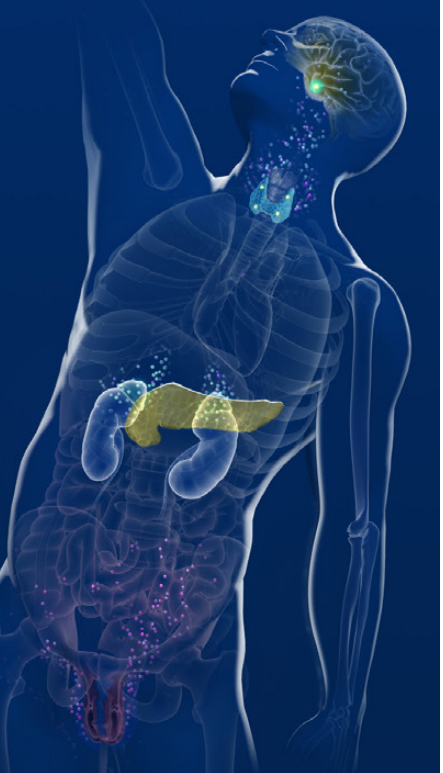
Jacksonville, Florida
800-634-1417

Rochester, Minnesota
800-533-1564

Resources

MayoClinic.org/medical-professionals

Clinical trials, CME, Grand Rounds, scientific videos and online referrals



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*.

21st Annual Nutrition and Wellness in Health and Disease 2021 — LIVESTREAM
Sept. 20-21, 2021
Nutrition, physical activity and other healthy-lifestyle behaviors are vital components in both the promotion of health and the treatment of disease. This program highlights ambulatory nutrition and wellness topics.

Principles in the Care of Transgender and Intersex Patients 2021
Oct. 21-23, 2021
Topics include medical, surgical, psychosocial, legal and ethical issues in transgender and intersex care. Participants leave with the skills to provide progressive and informed care to this emergent patient population.

2nd Annual Mayo Clinic Thyroid and Parathyroid Disorders Course 2021
Nov. 5-7, 2021
Review of imaging modalities and diagnostic methods such as molecular testing for evaluation of thyroid nodules, plus therapeutic options for the management of benign and malignant thyroid and parathyroid conditions.

MAYO CLINIC | mayoclinic.org

4500 San Pablo Road
Jacksonville, FL 32224

200 First Street SW
Rochester, MN 55905

13400 East Shea Blvd
Scottsdale, AZ 85259

MC5810-0121