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GUEST EDITORIAL

The Pulse of Progress: AI's Role in the Future of Health Care

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We have had access to artificial intelligence (AI) in medical care for many years, although until recently it may not have been so visible. AI algorithms already assist radiologists in identifying abnormalities or potential issues in medical images, speeding up diagnostic processes. AI has been used in decision support technology, robotic surgery, virtual medical chatbots, and to analyze pathology slides, helping pathologists identify and classify diseases more accurately and efficiently. However, there is no denying that something is different now.

The latest iterations of Al feel quicker, more familiar, and more ... intelligent. Tim Smith, an investor and journalist, describes disruptive technology as one that "sweeps away the system or habits it replaces" because of its superiority.[1] AI now has the potential to be one of the most disruptive technologies ever seen, and health care will not be immune.

In 1993, I bought a copy of *Internet for Dummies* and logged into various university data centers through my dial-up modem. Through TCP/IP protocols I downloaded a copy of the Netscape browser, installed the program, and saw my first glimpse of the internet graphics interface as we recognize it today. I had feelings of both awe and anxiety, as if I was stepping through a great entryway. Thirty years later, it is hard to imagine not having daily access to the internet and the impact it has on our lives.

On November 30, 2022, ChatGPT was launched by the San Francisco-based company OpenAI. This advancement in AI is different, evoking the same sense of potential and change that I felt in 1993. Key to this development have been advances in the structures behind the artificial intelligence, moving away from a rules-based architecture (symbolic AI) to one built on the structure and relationships between data (connectionist AI). This model is engineered on principles that govern neural networks in the human brain and becomes more intelligent through increased exposure to data by learning the patterns and relationships associated with it.

Several technologies have converged to allow for this leap to utilizing connectionist architecture, including advances in understanding regarding deep learning and neural networks, availability of large datasets, and most importantly exponential increases in computing power at lower costs. Large language model algorithms are used by AI to act on these large datasets to understand, summarize, generate, and predict new content. This has resulted in a "conversational" aspect to the AI that seems to understand context and nuance.

HOW COULD AI HELP US IN HEALTH CARE?

Various stakeholders, including health care companies and electronic medical record vendors, are busy exploring potential applications for the new AI. Artificial intelligence in health care holds the promise of transformative advancements, with increasingly sophisticated algorithms driving more personalized and precise medical interventions. Within the next decade we will likely witness revolutionary changes in the realms of diagnostics, drug discovery, and treatment strategies, leading to more efficient health care delivery and improved patient outcomes.

AI may likely streamline administrative processes, optimize diagnostics, and offer invaluable decision support to physicians. This shift could allow health care providers to spend more time at the patient's bedside, fostering a more personalized and compassionate approach to medicine. By automating routine tasks and synthesizing vast amounts of data, AI may not only enhance the efficiency of medical workflows but also augment diagnostic accuracy, leading to earlier detection of diseases and improved treatment outcomes.

AN OMINOUS POSSIBILITY

Can AI fully replace health care providers? Issues with legal, risk, acceptance, privacy aside, that future — at least from the "can we" perspective — is closer than we might think. An early-stage experimental model created by Google called Artificial Medical Intelligence Explorer (AMIE) demonstrated

the ability to outperform primary care providers in generating differential diagnoses as well as conveying empathy to actors portraying patients in a very small clinical trial. Med-PaLM 2 is a Google-designed AI model — currently only available for research — that has demonstrated the capacity to achieve an 85% score on medical licensing exams, far exceeding the score achieved by most practicing clinicians.[2]

Watch a video of some exciting advances in AI by scanning the QR code at right or by visiting youtube.com/watch?v=3BPzqH5sF90

AI currently can and should start to replace many of the administrative and repetitive tasks in medicine, as well as potentially provide more "rules-based" decision-making, including some medical triage, for example. This could lead to significant improvements in efficiency of care delivery.

However, there remain limitations in our ability to recreate areas of advanced human intelligence including common sense, emotional intelligence, consciousness, and ethical reasoning. Although advances are being made even in those areas, an inability of these as-yet uniquely human characteristics will continue to limit AI's ability to completely replace clinicians.

DATA ➔ INFORMATION ➔ KNOWLEDGE ➔ WISDOM

In our digital world, we are drowning in medical data, constantly struggling with good information and only dabbling with knowledge, making true wisdom ever elusive. While our approach has been to "search" for information, this amounts to casting a small net into a vast sea hoping to capture a few tidbits of knowledge. That strategy has been around since the early days of the internet (e.g., the dawn of the WebCrawler search engine) and has been tried (and has failed) within our own electronic medical records.

AI has the potential to revolutionize how we find and utilize information for patient care. The conversational aspects of AI may be the most intriguing. These can help us finally leverage the vast mine of medical data and put it to work for us. Consider these potential "asks" for our new AI:

- Generate a summary for me of this patient's most pertinent issues since their last visit, from the perspective of an anesthesiologist.
- Show me a list of all my patients currently most at-risk for a coronary heart disease event.
- Create a note for today's encounter in the context of a neurology visit.
- Given the information from today's visit and history over the past five years, generate a differential diagnosis list in order of likelihood with a summary of the lowest cost diagnostic tests needed for each.
- Based on today's note, generate an appropriate billing code and potential opportunities for additional documentation.

All these examples are technically possible today, and many will start to appear soon as our AI medical applications begin to integrate the data in our charts. At this time the technology is evolving fast and the developers are struggling to keep up.

WHAT COULD POSSIBLY GO WRONG?

Health care delivery is generally very inefficient, so the potential efficiency impact will be exponential. Yet, it is critical to acknowledge the potential pitfalls that will come with this technology.

The ethical aspects of AI in health care will demand vigilant oversight, particularly regarding issues of patient-data privacy, algorithmic bias, and the potential for overreliance on computer-generated recommendations. Regulatory frameworks are being established to address concerns related to bias, transparency, and accountability. Most notably, in January 2023 the National Institute of Standards and Technology released the AI Risk Management Framework, which provides a comprehensive approach to managing AI risks throughout the AI lifecycle, including those of safety, security, fairness, and accountability.

While governmental and industry bodies have begun to issue guidance around the safe development and use of AI, the industry is evolving too rapidly to keep up. There is a particular scarcity of oversight in health care apart from Food and Drug Administration regulations for clinical tasks related to diagnosis, treatment, or interpretation; regarding AI, there are only a handful of state-based legislations. Striking the right balance between human expertise and AI assistance will be critical to ensure that the provider's role evolves without diminishing the inherent essence of compassionate care.

Finally, the fear of job displacement among physicians and caregivers will be real as AI systems increasingly excel in tasks traditionally performed by medical professionals. It will be essential for the

medical community, policymakers, and technology developers to collaborate in shaping this future.

FINAL THOUGHTS

We are at the intersection of technology and patient care, witnessing the nascent impact of AI on the medical landscape. The future of AI in health care holds the promise of transformative advancements in medical treatment and process, leading to more efficient health care delivery and improved patient outcomes. However, privacy and ethical considerations, regulatory frameworks, and the continued collaboration between technology developers and health care professionals will be important for realizing the full potential AI can offer.

AI in health care will be a powerful, disruptive force, and dismissing its potential impact would be futile. It is the proverbial "freight train" coming down the track; we need to be actively involved in shaping the future and embrace the changes to come. It is important that clinicians help steer the development and use of AI to remain effective and relevant to providing care. This may take the form of local IT development, involvement in emergency medical record focus and user groups, and vocal support and criticism through medical societies or governmental forums.

Health care professionals bring empathy, ethical judgment, and personal experience, all critical to how we care for patients. Collaboration will ensure that AI systems will complement rather than replace the human elements of health care, leading to more holistic and effective health care impacts.

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JLGH Summer 2024 Recap

Q&A for Extended Learning

The Summer issue of The Journal of Lancaster General Hospital *offered articles on pharmacotherapeutic agents for the management of type 2 diabetes, urinary tract infections in women, and quality improvement and health equity, as well as a photo quiz on Henoch-Schönlein purpura and other practice recommendations. Review the questions and answers below to see how much you remember from the issue. Need a refresher? All issues of* JLGH *are available online at JLGH.org.*

Q A **Ultra-long-acting insulins are now available with similar efficacy to shorter acting formulations. What are some benefits of insulin degludec (U-100 and U-200) and insulin glargine (U-300)?**
Insulin degludec (U-100 and U-200) results in decreased rates of nocturnal hypoglycemia in clinical trials and a duration of action of up to 42 hours. Insulin glargine (U-300) allows for decreased injection volumes and a duration of action of up to 36 hours.

Q A **Henoch-Schönlein purpura (HSP) generally occurs in children and teens 3-15 years of age and presents as palpable purpura with acute abdominal pain. What is the treatment for HSP?**
Supportive care includes having patients stay well hydrated, plus using NSAIDs for joint pain and prednisone for more concerning symptoms. Frequent monitoring of kidney function is important; kidney biopsy is warranted in severe cases.

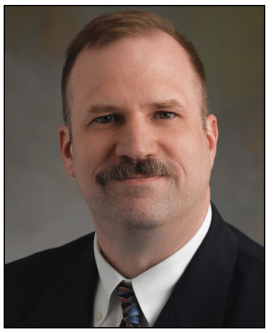
Q A **Why might we consider treating dyspareunia in women with antibiotics?**
Up to 80% of women of reproductive age with dyspareunia may have an undiagnosed urinary tract infection (UTI). While patients who are perimenopausal and postmenopausal more often have genitourinary syndrome than UTI, 94% of women with UTI-associated dyspareunia respond positively to antibiotics.

Q A **Penn Medicine economist Rachel Werner, MD, PhD, suggests four approaches to modifying health care's value-based payment program to advance health equity. What might these include?**
Create accountability for equity, account for social risk in performance management, financially support under-resourced providers, and address drivers of inequity.

A Case-Based Approach to Thrombocytopenia in Adults

Part 1: Differential Diagnosis

Brennan



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Thrombocytopenia is a vast topic ranging from lab artifacts like pseudothrombocytopenia to immediately life-threatening events such as microangiopathic hemolytic anemia. This case-based discussion demonstrates some key aspects of several common and uncommon causes of thrombocytopenia in adults and will be presented in two parts. The etiologies, which will be outlined in more detail in Part 2, can broadly be thought of as either decreased production or increased consumption.

Formulating the differential diagnosis necessitates keeping the acuity of the illness and the severity of the thrombocytopenia in mind (see Fig. 1). Once the provider has resolved that the thrombocytopenia is not emergent, the differential diagnosis can be focused using data from further lab and clinical studies.

Evaluation for new medications, recent illness, and travel are important. Chronic conditions such as cancer or chronic liver disease, as well as a history of gastric bypass surgery, can result in lower platelet counts. Lab testing often includes B_{12}, folate, HIV, and hepatitis C. If this workup is unrevealing, providers can consider using ultrasound to evaluate for splenomegaly, performing a bone marrow aspiration and biopsy for underlying hematologic malignancies, as well as checking serum copper (noting low serum copper levels can be seen in Wilson's disease, which is a copper overload state). Finally, if all testing is unremarkable, one could consider genetic testing for inherited platelet disorders in the right clinical context.

CASE 1: A 67-year-old male presents with a longstanding history of thrombocytopenia and the following labs.

WBC Count (4.8-10.8 10*3/µL)	**6.3**
RBC Count (4.60-6.20 10*6/µL)	**5.08**
Hgb (14.0-18.0 g/dL)	**14.9**
Hct (40.0-54.0%)	**43.3**
MCV (80.0-100.0 fL)	**85.2**
MCH (27.0-33.0 pg)	**29.3**
MCHC (32.0-36.0%)	**34.4**
RDW (12.2-14.6%)	**13.5**
Platelet Count (150-450 10*3/µL)	**83▼**
Neutrophils Absolute (2.20-8.00 10*3/µL)	**3.43**
Lymphocytes Absolute (0.90-5.00 10*3/µL)	**2.32**
Monocytes Absolute (0.20-1.10 10*3/µL)	**0.41**
Eosinophils Absolute (0.00-0.40 10*3/µL)	**0.07**
Basophils Absolute (0.00-0.40 10*3/µL)	**0.02**

On repeat, the following comment was made: "unable to perform accurate platelet count because platelets clump in ethylenediaminetetraacetic acid (EDTA)." Sending a sample in a sodium citrate tube results in a normal value.

Preanalytic variables can affect platelet counts and can create a clotted specimen (i.e., a collection that was not adequately mixed). This occurs when an antico-

	EVALUATION
• TTP (Thrombotic Thrombocytopenic Purpura) • HUS (Hemolytic Uremic Syndrome) shiga toxin or complement mediated	Normal coagulation studies Hemolysis ↑LDH ↑Reticulocytes ↑Indirect bilirubin ↓Haptoglobin
• HELLP (Hemolysis Elevated Liver enzymes Low Platelets)	
• DIC (Disseminated Intravascular Coagulopathy)	↓Fibrinogen; prolonged PT/PTT
• HIT (Heparin-Induced Thrombocytopenia)	Heparin exposure; anti-platelet 4 antibodies with reflex serotonin release assay
• Acute Leukemia	Bone marrow biopsy
• CAPS (Catastrophic Antiphospholipid Antibody Syndrome)	ACA, AB2gp1, LAC; history of autoimmune disorder
• ITP (Immune Thrombocytopenia Purpura)	Diagnosis of exclusion
• D-ITP (Drug-Induced ITP)	New medication
• PTP (Post Transfusion Purpura)	Platelet transfusion 5-10 days prior

Fig. 1. Differential diagnosis and associated evaluation for sick patients with thrombocytopenia.
ACA = anticardiolipin antibody, AB2gp1 = anti-beta 2 glycoprotein 1 antibody, LAC = lupus anticoagulant, LDH = lactate dehydrogenase.

agulant, typically EDTA, exposes a platelet membrane epitope, resulting in platelet clumping (see Fig. 2) due to immunoglobulin recognition (often to glycoprotein IIb/IIIa).[1] This clumping has no clinical significance, as it is purely an in vitro phenomenon causing erroneous automated platelet counts; clumps may be mistaken for white blood cells.

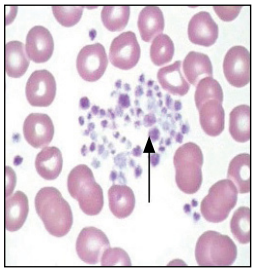

Fig. 2. Platelet clumping in EDTA in Case 1.

This phenomenon occurs in 0.1% of EDTA anticoagulated tubes.[2] It is recognized by reviewing a peripheral smear demonstrating the clumping and confirmed by switching to an alternative anticoagulant such as sodium citrate, heparin, or acid citrate dextrose, which results in a normal platelet count. If those attempts fail, however, providers can attempt running a fingerstick sample at bedside — making a peripheral smear without using an anticoagulated tube and estimating total values based on a manual count. Patients should be educated to inform health care professionals regarding this issue so that future tests are conducted using the appropriate anticoagulated sample.

Diagnosis: pseudothrombocytopenia

• If platelet clumping is noted, send a sample in a sodium citrate tube.

CASE 2: A 75-year-old male presents with a history of cirrhosis secondary to nonalcoholic steatohepatitis (NASH) complicated by portal hypertension and nonbleeding esophageal varices. He has the following labs and coronal CT abdominal imaging (see Fig. 3). The B_{12}, folate, and copper levels are unremarkable.

WBC Count (4.8-10.8 10*3/µL)	**4.7▼**
RBC Count (4.60-6.20 10*6/µL)	**4.37▼**
Hgb (14.0-18.0 g/dL)	**14.3**
Hct (42.0-52.0%)	**42.0**
MCV (80.0-100.0 fL)	**96.1**
MCH (27.0-33.0 pg)	**32.7**
MCHC (32.0-36.0%)	**34.0**
Platelet Count (150-450 10*3/µL)	**73▼**
Neutrophils Absolute (2.20-8.00 10*3/µL)	**2.82**
Lymphocytes Absolute (0.90-5.00 10*3/µL)	**1.08**
Monocytes Absolute (0.20-0.80 10*3/µL)	**0.56**
Eosinophils Absolute (0.00-0.40 10*3/µL)	**0.19**
Basophils Absolute (0.00-0.40 10*3/µL)	**0.03**
Immature Granulocyte Absolute (0.00-0.22 10*3/µL)	**0.01**

Splenic sequestration is a common finding among those with hypersplenism (normal spleen size is commonly defined as less than 12 cm, although taller individuals and men can be slightly larger than this and be normal).[3] Although the peripheral concentration of platelets is reduced, the total body platelet mass remains normal.[4] Therefore, bleeding does not typically correlate to the platelet concentration in hypersplenism, but rather some additional factor such as esophageal varices, coagulation factor derangements, or acquired platelet dysfunction in the setting of cirrhosis.

Two-thirds of those with cirrhosis will have thrombocytopenia, but only one in eight will have thrombocytopenia between 50,000/µL and 75,000/µL. Additional causes of thrombocytopenia can coexist and can include nutritional deficiencies, bone marrow suppression from medications, hepatitis C, reduced liver production of thrombopoietin (TPO), or underlying bone marrow disorders like myelodysplastic syndromes, among others.[5] Therefore, a platelet concentration <75,000/µL should raise suspicion for something beyond sequestration. Platelet transfusion in an acute setting or the use of TPO mimetics such as avatrombopag can be effective ways to raise platelet counts in cirrhosis and splenic sequestration.[6]

Diagnosis: splenic sequestration

• Thrombocytopenia <75,000/µL in cirrhosis should prompt consideration of alternative causes.

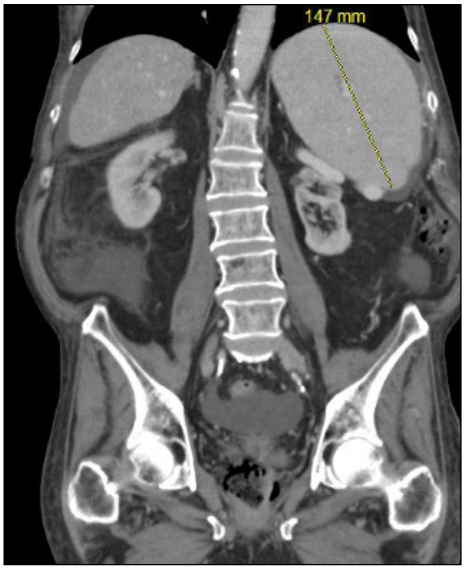

Fig. 3. Coronal reformatting of CT abdomen/pelvis with intravenous contrast demonstrating splenomegaly in Case 2.

CASE 3: A 55-year-old male with no recent medical care presents to the Emergency Department with severe sepsis due to *Streptococcus intermedius bacteremia.* CT imaging of the abdomen and pelvis demonstrates right hepatic and infrahepatic inferior venal canal thrombi as well as indeterminate hepatic masses, which

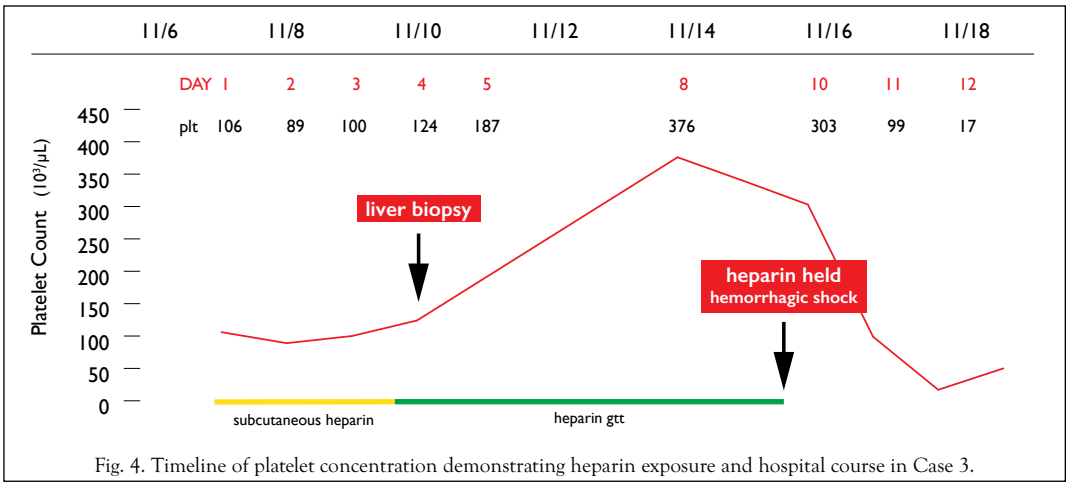

Fig. 4. Timeline of platelet concentration demonstrating heparin exposure and hospital course in Case 3.

are possibly abscesses. This prompts treatment with piperacillin/tazobactam and prophylactic heparin. The patient is started on a therapeutic heparin drip on day four after a liver biopsy was performed. On day nine, he develops shock secondary to hemorrhage into the liver, and heparin is held. Four doses of platelets and three units of packed red blood cells are transfused. At that time, the biopsy results determine the patient has an abscess.

Platelets at the time of admission are 106,000/μL. The time course of platelet concentrations is shown in Fig. 4, with a peak platelet on day eight at 376,000/μL; the platelet counts undergo a precipitous drop thereafter. Platelets did not recover despite appropriate measures, prompting the hematology consult on day 11.

This case illustrates that there should be a broad differential for thrombocytopenia. Timing of heparin exposure in relation to platelet drop should be considered when approaching all cases of thrombocytopenia. It is worth noting that platelets should recover about two or three days after an acute bleed or surgical procedure — that is, consumption should not last beyond two to three days of the acute event (provided bleeding has been controlled) and should alert the clinician to consider heparin-induced thrombocytopenia (HIT).

While critically ill patients may have more than one cause of thrombocytopenia, the pretest probability for HIT can be determined by using the 4T score (see Table 1).[7] A normal platelet count is not sufficient to rule out the possibility of HIT if there has been a 50% drop from baseline 5-10 days after heparin exposure (or within the first five days of exposure if there has been heparin exposure in the preceding 100 days). For example, a reactive thrombocytosis and a platelet count on admission of 500,000/μL may drop to 250,000/μL (still within the normal range) on day seven following heparin exposure. This scenario should prompt a consideration of HIT.

This patient had a drop in platelets between days nine and ten coinciding with hemorrhage. Furthermore, he was on broad-spectrum antibiotics, which can suppress the bone marrow production of platelets or cause drug-induced thrombocytopenia around day seven to ten of exposure. Thus, many possible etiolo-

Table 1. 4T Score

4Ts	2 points	1 point	0 points
Thrombocytopenia	Platelet count fall >50% and nadir ≥20,000/μL	Platelet count fall 30% to 50% or nadir 10,000-19,000/μL	Platelet count fall <30% or nadir <10,000/μL
Timing of fall	Clear onset between days 5-10 or ≤1 day (prior heparin in last 30 days)	Consistent with days 5-10, but not clear (missing platelet counts): onset > day 10; or fall ≤1 day (prior heparin in last 30-100 days)	Platelet count fall <4 days without recent exposure
Thrombosis or other sequelae	New proven thrombosis, skin necrosis, acute anaphylactoid reaction to heparin	Progressive/recurrent thrombosis, non-necrotizing (erythematous) skin lesions, suspected thrombosis (not proven)	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

A score of 0-3 suggests low pretest probability for HIT, 4-5 suggests intermediate pretest probability, and 6 or more suggests a high pretest probability of HIT. Testing anti-platelet factor 4 antibodies with reflex serotonin release assay is indicated for intermediate or higher scores, and alternative anticoagulants are recommended. *Adapted from Lo et al.*[7]

gies could explain this thrombocytopenia. The 4T score, however, gave an intermediate pretest probability of HIT with four points: one point for nadir platelet count 10,000-19,000/µL, two points for timing within days five to ten and no recent heparin exposure, zero points for no attributed thrombotic event, and one point for possible other causes of thrombocytopenia. This prompted further testing.

An anti-platelet factor 4 antibody optical density was extremely high at 2.9, and a confirmatory serotonin release assay (SRA) was positive. Thus, the diagnosis of HIT was confirmed. Anti-platelet factor 4 antibody testing has a high sensitivity and thus a good negative predictive value if low, but there were many reasons for false positives; SRA is a more specific test and therefore can confirm the diagnosis.[8] Other testing platforms exist, but this approach is the most commonly used.

The incidence of HIT correlates with higher dosages of unfractionated heparin. It can occur in the setting of low molecular weight heparins, but it is less common with those agents than with unfractionated heparin. Orthopedic, surgical, and trauma patients are at higher risk of developing HIT compared to medical patients.[8] If one has had heparin exposure in the preceding 100 days, acute HIT can occur within the first 24 hours of repeat exposure. HIT should be a consideration even without concurrent thrombocytopenia in patients with necrotic skin reaction to the heparin product or anaphylactoid reaction to heparin administration.[8]

Stopping all heparin exposure is essential, including subcutaneous and intravenous doses as well as exposure from heparin flushes/locks and low molecular weight heparins. It is then critical to switch to an alternative anticoagulant (bivalirudin, argatroban, direct oral anticoagulants, warfarin, fondaparinux) unless medically contraindicated. HIT is extremely thrombogenic. Since it takes three months to clear platelet-activating antibodies, anticoagulation should be continued for at least three months.[9-11]

Direct oral anticoagulants (DOACs) are increasingly used due to their rapid onset and effectiveness, although they are not appropriate for all patients in the critically ill setting due to their longer half-lives compared to bivalirudin and argatroban. HIT can precipitate disseminated intravascular coagulation (DIC) and prolong partial thromboplastin time (PTT); bivalirudin and argatroban can confound PTT results. DOACs do not have this effect.[12]

Although warfarin can be used, one must be cautious due to its initial prothrombotic effects, and it should not be started until platelet recovery on an alternative agent.[13] For this reason, vitamin K reversal would be considered for those recently started on warfarin when diagnosed with HIT.

Heparin-independent anti-platelet 4 antibody disorders — autoimmune (heparin-independent) HIT and vaccine-induced immune thrombotic thrombocytopenia — are beyond the scope of this discussion; these may be considered in patients who have not received heparin products. Initial management is also similar, and intravenous immunoglobin (IVIG) may be useful for refractory cases.[12]

Diagnosis: heparin-induced thrombocytopenia

- If recent heparin exposure and a drop in platelet count, perform a 4T score. For intermediate/high-risk cases, send anti-platelet factor 4 antibody with reflex serotonin release assay and switch to alternative anticoagulant.
- A normal platelet count is not sufficient to rule out HIT if there is a 50% drop from peak.
- Anaphylactoid reaction to heparin raises suspicion of HIT.
- Platelets should start recovering two to three days after surgery; if not, consider HIT.
- HIT can be associated with DIC and prolonged PTT, which can affect titration of argatroban and bivalirudin.

CASE 4: A 36-year-old male presents with several weeks of bleeding gums and progressive lower extremity petechiae (see Fig. 5). His primary care physician finds he has severe thrombocytopenia.

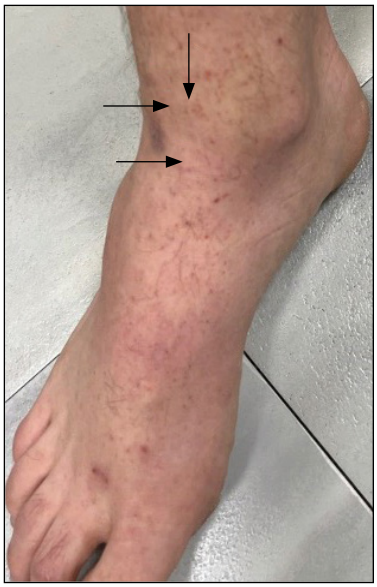

Fig. 5. Lower extremity petechiae, several identified by arrows, in Case 4.

He has the following labs.

WBC Count (4.8-10.8 10*3/µL)	6.3
RBC Count (4.60-6.20 10*6/µL)	4.17▼
Hgb (14.0-18.0 g/dL)	12.5▼
Hct (42.0-52.0%)	35.7▼
MCV (80.0-100.0 fL)	85.6
MCH (27.0-33.0 pg)	30.0
MCHC (32.0-36.0%)	35.0
Platelet Count (150-450 10*3/µL)	1.0▼
Immature Granulocyte (0.0-2.0%)	0.6
Neutrophils Absolute (2.20-8.00 10*3/µL)	4.48
Lymphocytes Absolute (0.90-5.00 10*3/µL)	1.27
Monocytes Absolute (0.20-0.80 10*3/µL)	0.31
Eosinophils Absolute (0.00-0.40 10*3/µL)	0.13
Basophils Absolute (0.00-0.40 10*3/µL)	0.03
Immature Granulocyte Absolute (0.00-0.22 10*3/µL)	0.04
Reticulocyte Count (0.5-2.5%)	3.9▲
INR (PT) (0.9-1.1)	1.0
PTT (23.0-31.6 s)	27.0
Vitamin B12	579
Folate Serum	16.7
GFR	>60
Glucose (serum)	104▲
Sodium	139
Potassium	3.9
Chloride	105
CO_2 Venous	27.5
Anion Gap	7
Blood Urea Nitrogen	12
Creatinine	1.1
BUN/Creatinine Ratio	11
Calcium	9.6
Calcium Corrected (Adj/Calc) Total	8.9
Protein Total Serum	7.5
Albumin	4.9
Globulin	2.6
A/G Ratio	1.9
Bilirubin Total	1.0
Alkaline Phosphatase	60
Lactate Dehydrogenase	293▲
AST (SGOT)	22
ALT (SGPT)	18
Haptoglobin	<30▼

He lives in the suburbs, has not recently traveled or gone hiking, and denies any known tick bites, recent viral illness, or diarrhea. He has no new medication or supplement exposure and denies illicit drug use. Labs done several years ago demonstrated a normal complete blood count and differential.

The anemia raises the possibility of a microangiopathic hemolytic anemia, which prompts additional lab evaluation. This reveals an elevated lactate dehydrogenase (LDH) and reticulocyte count, and a low haptoglobin consistent with hemolysis. Coagulation testing is normal, and direct antigen testing (DAT) is negative. A peripheral smear shows absolute thrombocytopenia with spherocytes, a normal white cell count, and an absence of schistocytes. Computed tomography of the chest, abdomen, and pelvis with intravenous dye shows splenomegaly (diameter = 17 cm) without adenopathy.

Spherocytes in the setting of hemolysis with thrombocytopenia raises the possibility of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS). However, an ADAMTS13 activity level is normal, and the patient has no stigmata of TTP/HUS. On further questioning, he relates that his sister has a history of hereditary spherocytosis, which is likely the cause of his acute and mild hemolysis. Furthermore, DAT is negative, making Evan's syndrome — concurrent immune thrombocytopenia purpura (ITP) and warm autoimmune hemolytic anemia — unlikely.

A clinical diagnosis of ITP is made. The patient is started on dexamethasone 40 mg daily for four days, with intravenous immunoglobin for two days. He has an initial platelet response but subsequent relapse; thus, he is treated with weekly rituximab for four weeks and achieves ongoing remission for several years (see Fig. 6).

ITP is a diagnosis of exclusion that requires quickly evaluating for other severe and life-threatening causes of severe thrombocytopenia. TTP, HUS, DIC, HELLP (hemolysis, elevated liver enzymes and low platelets), CAPS (cryopyrin-associated autoinflammatory syndromes), acute leukemia, and tickborne illnesses should be included in the differential. ITP can be primary (autoimmune), secondary to another condition (e.g., viral infection, autoimmune disorder, chronic lymphocytic leukemia), or drug induced. The incidence is 100 per one million. In children, ITP is often self-limited, while in adults it can have a relapsing and chronic course.[14]

Evaluation for presumptive ITP should include a travel history and whether there has been exposure to

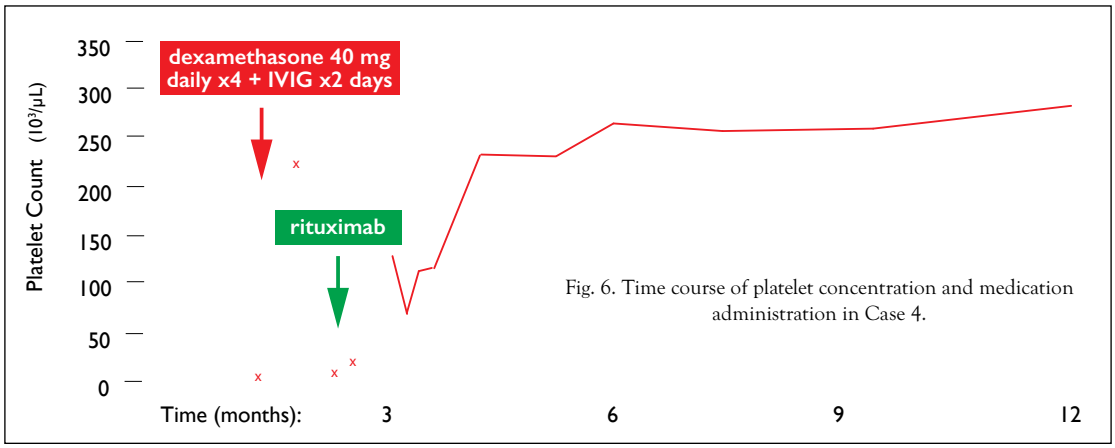

Fig. 6. Time course of platelet concentration and medication administration in Case 4.

ticks, recent viral infections, new medications, or herbal supplements. Workup should include testing for HIV, hepatitis C, and hepatitis B. Regarding the latter, it is critical to send hepatitis B core antibody (HBcAb) testing prior to administering IVIG, as passive antibody transfer will likely occur. Patients with HBcAb-positive serology need to undergo hepatitis B virus suppression if rituximab is ultimately needed, because CD20 depletion can result in fulminant hepatitis B.

Comparison to a patient's historic complete blood count if available will help to identify hereditary thrombocytopenia, which may help identify May-Hegglin anomaly or type 2B von Willebrand disease.

Treatment of ITP depends on the severity of the thrombocytopenia, as well as the clinical scenario. The goal platelet concentration is greater than 30,000/μL unless there is bleeding or the patient needs an invasive procedure. Therefore, some patients can be monitored without intervention as outpatients.

In those with newly diagnosed ITP and a platelet count <20,000/μL, admission to the hospital is recommended. If there is no urgent need to raise the platelets, steroids can be initiated — a dexamethasone pulse of 40 mg daily for four days or prednisone 0.5-2 mg/kg daily to be tapered off within six weeks should be initiated. It may take two to three days for platelets to begin responding. In those with active bleeding or bruising or platelet counts of <10,000/μL, IVIG may be more appropriate, as responses occur within 12-24 hours.

If there is life-threatening or serious bleeding, platelet transfusions may be considered; however, these may also be rapidly cleared by the immune process. Refractory or relapsing cases can be treated with rituximab or thrombopoietin receptor agonists such as eltrombopag or romiplostim. Some patients may experience a spontaneous remission within the first year, so splenectomy is reserved for refractory cases that last more than one year.[15] Additional evidence is emerging for anti CD38 monoclonal antibodies as well.[16]

Diagnosis: immune thrombocytopenia purpura with hereditary spherocytosis

- ITP is a diagnosis of exclusion.
- Initial treatment includes steroids +/- IVIG.
- Historical platelet count is helpful, as inherited thrombocytopenia can mimic ITP.

CONCLUSION

As these cases demonstrate, the differential diagnosis for thrombocytopenia can be broad and complex. Understanding the differential will allow a clinician to consider life-threatening etiologies and initiate the appropriate workup and treatment. In Part 2, we will present additional cases that illustrate the approach to thrombocytopenia in adults.

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Caring for Gender-Diverse Patients

Gender-Affirming Hormone Therapy

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INTRODUCTION

People who are transgender, gender diverse, or gender non-conforming have a gender identity that differs from their sex assigned at their birth. A recent study done by the Pew Research Center shows that 1.6% of American adults identify as transgender or nonbinary, and among young adults 18-29 years of age, it is even more common, at 5.1%.[1]

Gender-diverse people have high rates of health disparities, including higher rates of human immunodeficiency virus (HIV), substance use, mental health disorders, and victimization, much of which is attributable to minority stress; as opposed to stress that is experienced by everyone, minority stress has its roots in stigma and prejudice.[2] Suicide risk is high in gender-diverse populations: between 22% and 43% of transgender people have attempted suicide in their lifetime.[3] Importantly, good social support mitigates some of this risk — in one study of trans youth 16-24 years of age, the risk of suicide attempt in individuals with strongly supportive parents was 4% compared to 57% in those with somewhat supportive to not-at-all supportive parents.[4]

In addition, gender-diverse individuals face significant discrimination in medical settings. According to a study performed in 2022 by the Center for American Progress, 16% of transgender respondents reported that their provider used harsh/abusive language and 10% reported providers refusing to see them. There are challenges outside of discrimination, as well — a lack of training in gender-affirming care means that 30% of transgender respondents reported having to teach their provider about their gender so they receive appropriate medical (not even necessarily gender-affirming) care.[5]

Ample evidence shows that gender-affirming hormone therapy (GAHT) improves mental health outcomes for appropriate patients.[6,7]

How does a provider assess whether an adult patient is a good candidate for GAHT?

According to the World Professional Association for Transgender Health (WPATH) Standards of Care, the following are needed to begin gender-affirming hormone therapy in adults 18 years of age and older:

1. Patients should have marked and sustained gender incongruence — typically defined as being at least six months in duration.
2. Patients should have the ability to consent to starting hormone therapy and understand the potential impact on reproductive options.
3. Patients should have appropriate co-management of mental health conditions and physical health conditions that could negatively impact the outcome of treatments.[8-10]

In addition, a comprehensive medical, behavioral, social, gender, and sexual history should be obtained (see Table 1). Relevant physical exam steps should be completed; a genital exam is generally not necessary prior to initiating treatment.

In this article, we will review two fictionalized patient cases to introduce providers to prescribing

gender-affirming hormone therapy for adults. Both patients meet WPATH criteria for initiating GAHT. Prescription of GAHT for adolescents is beyond the scope of this article. These cases in no way encompass the wide variety of experiences and identities lived by gender-diverse persons but seek to teach some basic principles. Every patient may have different goals. It is worth noting that for some persons who may not want a drastic change in their physical appearance, hormone therapy should be started at a low dose and titrated slowly.

CASE 1: AH

AH is a 28-year-old patient who presents as a new patient to a primary care office to discuss gender-affirming hormone therapy. AH identifies as a transgender (or "trans") woman and uses she/her pronouns. She had a male sex assigned at birth.

AH has known since early childhood that something was different about how she felt in her body. As a young child, she had more traditionally "feminine" interests and got along better with other young girls. She would frequently ask her parents if she could become a girl, but stopped when it was clear this was upsetting her parents.

During puberty, she experienced extreme distress at her pubertal changes. She started to experience severe depression in her adolescent years, culminating in a suicide attempt and psychiatric hospitalization at age 16 years.

She first identified as trans at age 18 years, after learning about the trans community and realizing that the concept of being transgender finally explained how she had been feeling. She started identifying as a woman at that time to supportive friends but was not "out" to her family due to concerns about her safety while living at home. In her mid-20s, with the help of a supportive gender-affirming therapist, she started living independently and had improvement in her depression. She started identifying as a woman to those around her, growing out her scalp hair, doing laser removal of her facial and body hair, and experimenting with more "feminine" clothes.

She has developed a strong support system with friends, a long-term partner, and a few supportive family members. She presents at this time to discuss gender-affirming hormone therapy. She strongly desires the development of breasts, a more "feminine" body shape, a more "feminine" voice, and the reduction of facial and body hair. She does not want biological children.

What medications would you use for gender-affirming hormone therapy for AH?

The most common medications used would be estradiol and an antiandrogen. A common starting dosage would be estradiol oral 2 mg daily and spironolactone oral 50 mg daily.[9,10]

The goals of these medications are to further develop "feminine" secondary sex characteristics and suppress or minimize "masculine" secondary sex characteristics.[9,10] The expected effects and timeline of secondary sex characteristic development are listed in Tables 2 and 3 on page 76. Patients should be informed that it may take months to start seeing the effects of GAHT and that maximal effect can take three to five years. Providers should review the expected effects of the medication, timeline to effect, and potential adverse effects with patients before initiating therapy. Of note: most of the potential side effects from estrogen and antiandrogen therapies are

Table 1. Recommended History and Physical Exam for Gender-Affirming Hormone Therapy Assessment[9,10]

Gender Identity History
• History of experienced gender awareness and the development, exploration, and persistence of that gender
• Desire for future fertility
Medical History
• Personal history of arterial or cerebrovascular disease, arterial or venous thromboembolism, hypertension, hormone-sensitive cancer, polycythemia, pituitary adenoma, liver disease, HIV infection, and other sexually transmitted infections
• Prior use of prescribed or unprescribed hormone therapy or surgical procedures
Behavioral Health History
• History of mental health diagnoses and treatment, psychiatric hospitalizations, past or present suicidality
Family History
• Family history of any cancer, cardiovascular disease, diabetes, or blood clotting disorders
Social History
• Family, chosen family, history of rejection and acceptance
• Living situation and safety
• Sexual history, sexual orientation
Physical Exam
• Genital exam at first visit usually not necessary
• Anatomic inventory of organs present to guide organ-appropriate screenings (pap smear for persons with a cervix, mammogram for persons with breasts, discussion of prostate screening for persons with prostates)

similar to the potential health risks seen in cisgender women — that is, a woman whose gender matches their sex assigned at birth.

Providers should ensure special attention is paid to discussing fertility effects — gender-affirming hormone therapy may cause potentially permanent infertility. Anyone desiring future fertility should be referred to a fertility specialist prior to starting GAHT.

Oral estradiol is the most commonly used formulation of estradiol due to cost and ease of use (see Table 4). The preferred estrogen formulation is 17-beta estradiol rather than ethinyl estradiol (commonly used in oral contraceptives) or conjugated estrogens (often used to treat menopausal symptoms); the latter two would impose a higher thrombotic risk. Providers should consider use of transdermal estradiol for patients who have risk factors for atherosclerotic cardiovascular disease or venous thromboembolism as it confers a lower thrombotic risk than oral or injectable formulations.

Spironolactone is the most commonly used antiandrogen as it has a stronger antiandrogenic effect than the 5-alpha reductase inhibitors. 5-alpha reductase inhibitors may be more effective for patients with significant alopecia or patients who cannot tolerate spironolactone. The 5-alpha reductase inhibitors block the conversion of testosterone to its more potent form, dihydrotestosterone (DHT).

GAHT is not an effective contraceptive on its own. Patients who are sexually active with someone who can get pregnant should ensure contraception is used.

What lab testing should be done prior to starting GAHT?

A comprehensive metabolic panel should be completed prior to starting spironolactone.

Table 2. Effects of Estrogen/Antiandrogen Therapy[9,10]

Expected Effects	Adverse Effects
Potentially Permanent • Breast growth • Decreased size of testicles ***Typically Reversible*** • Loss of muscle mass • Fat redistribution from abdomen to buttocks, hips, and thighs • Softening of skin • Decreased facial and body hair growth • Slowed androgenic hair loss • Reduced sex drive and decreased strength of erections	***Estradiol*** • Nausea (most common) • Increased risk of VTE, although overall risk remains low; transdermal estradiol safer for those at higher risk • Potentially permanent infertility — time to infertility and permanence varies greatly person-to-person • Possible increased risk of cardiovascular disease • Possible increased risk of hypertension, gallbladder disease, worsening of existing liver disease, migraines, and prolactinoma • Somewhat increased risk of breast cancer compared to cisgender men (although still significantly decreased compared to cisgender women) ***Any Antiandrogenic Medication*** • Erectile dysfunction and decreased sex drive (sildenafil and tadalafil may be used if needed) ***Spironolactone*** • Polydipsia, polyuria, and orthostasis • Rarely hyperkalemia and renal dysfunction — caution in those with preexisting renal disease or use of ACE inhibitor, ARB, or loop diuretic

VTE = venous thromboembolism, ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker

Table 3. Timeline of Changes After Estrogen/Antiandrogen Therapy Initiation (earliest onset to maximal effect)[9,10]

	1mo	3mo	6mo	1yr	2yr	3yr	4yr	5yr
Decreased spontaneous erections	■	■	■	■				
Decreased libido	■	■	■	■				
Decreased testicular volume		■	■	■	■	■		
Breast growth		■	■	■	■	■		
Decreased sperm production		approx.	■	■	■	■	■	■
Decreased muscle mass		■	■	■	■			
Fat redistribution		■	■	■	■	■		
Decreased hair growth			■	■	■	■	■	■

What lab testing should be done to monitor efficacy of GAHT in this patient?

Typically, total testosterone, estradiol, and a basic metabolic panel should be checked every three months while titrating therapy and then yearly thereafter. A pregnancy test is not necessary.

Goal estradiol levels for patients seeking full feminizing effect are typically in the natal female range of 100-200 pg/ml. Goal testosterone levels are typically less than 55 ng/dl. If patients are on injectable therapy, levels should be checked mid-cycle.[9,10]

CASE 2: PW

PW is a 22-year-old patient seeking gender-affirming hormone therapy. He identifies as transmasculine and uses he/they pronouns. He had a female sex assigned at birth.

PW states that they never felt "right" in their body ever since early childhood. He was always quite sporty, called a "tomboy," but never felt like that label fit correctly. His parents remember that he was extremely distressed when he had to wear dresses growing up and when people described him and his sisters as "the girls of the family." Starting in early adolescence, he was able to identify that he did not feel like a girl inside.

He started puberty at an early age and started menstruating at age 11. He felt severe dysphoria related to breast growth and menstruation. He had significant depression in early adolescence and was later diagnosed with bipolar 2 disorder at age 16. He was started on lamotrigine, and his mood has been stable on this medication since then.

He has a generally supportive family and came out as gender fluid at age 14 to friends and family, meaning he had a gender identity that was not fixed. As he then explored his gender identity further, he came out as transmasculine around age 18, meaning he identified as masculine, although not necessarily male. He tends to dress in more androgynous clothes and binds his breasts daily.

He has been doing voice training online to try to develop a more "masculine" voice. He is interested in gender-affirming hormone therapy, with the goal of developing a more "masculine" body shape, stopping menstruation/monthly bleeding, and developing body/facial hair growth. He thinks he is interested in top surgery in the future. He does not think he wants biological children but would like to talk to a fertility specialist to discuss options before deciding, and he is referred to a fertility specialist before initiation of GAHT.

What medication would you start for gender-affirming hormone therapy for this patient?

The most commonly used medication in this setting is testosterone, which is most often administered via injection. A typical starting dose may be testosterone cypionate 50 mg subcutaneous once weekly.[9,10]

The goal of androgenizing therapies is to develop more "masculine" secondary sex characteristics and to suppress or minimize "feminine" secondary sex characteristics. The expected effects and timeline of

Table 4. Dosage Chart for Commonly Used Medications[9,10]

Formulation	Name	Dose Frequency	Low Dose	Common Dose	Max Dose	Med Notes
Oral	Estradiol tablet	Daily to twice daily	1-2 mg	4-6 mg	8 mg	Cheap and easy to administer.
Transdermal estradiol patches	Climara	Weekly	0.05 mg	0.1-0.2 mg	0.4 mg	Lowest thromboembolic and cardiovascular risk; difficult to get more than two patches to be covered by insurance at a time.
	Vivelle-Dot	Twice weekly				
Injectables *Intramuscular*	Estradiol valerate	Every 2 weeks	5 mg	10-15 mg	30 mg	Can also be given weekly — cut dose in half if dosing weekly. May have wider fluctuations in hormonal levels than other formulations. Learning to inject hormones is an additional skill patients must learn.
	Estradiol cypionate	Every 2 weeks	1.5 mg	3-6 mg	10 mg	
Antiandrogens						
Spironolactone	Spironolactone	Once to twice daily	25 mg BID	50-100 mg QD-BID	200 mg BID	
5-alpha-reductase inhibitors	Finasteride	Daily	1 mg	1-5 mg	10 mg	
	Dutasteride	Daily	–	0.5 mg	0.5 mg	

development on secondary sex characteristics are listed in Tables 5 and 6.

Patients should be informed that it may take months to start seeing the effects of GAHT and that maximal effect can take three to five years to develop. Providers should review the expected effects of the medication, timeline to effect, and potential adverse effects with patients before initiating therapy. Of note: most of the potential side effects from testosterone are similar to potential health risks seen in cisgender men. Providers should discuss the potentially permanent fertility effects of these medications.

Several formulations are available and effective (see Table 7). The most commonly used formulation for testosterone administration is injectable testosterone, which has a low cost and increases testosterone quickly and efficiently. Transdermal testosterone is also commonly used and may produce a steadier state of hormone levels but a slightly more gradual physical change.

Androgenizing therapy is not reliable contraception for individuals capable of pregnancy; therefore, pregnancy testing should always be a consideration as needed, and counseling regarding pregnancy and contraception is essential. No forms of birth control are absolutely contraindicated; however, combined estrogen-progesterone forms of birth control might interfere with androgenizing therapy.

What testing should be done at baseline for PW?

Baseline testing should include hematocrit and pregnancy testing if pregnancy is possible.

What follow-up testing should be done for this patient?

Typically, total testosterone and hematocrit should be assessed every three months while titrating therapy and then yearly. Pregnancy status should be checked as indicated. Goal total testosterone levels for patients seeking full masculinizing effect are typically in the upper end of the normal cisgender male range, 650-1,000 ng/dl. If patients are on injectable therapy, the level should be checked mid-cycle.[9,10]

At follow-up visits for patients on GAHT, providers should assess adherence, barriers to getting medications, and side effects. Providers should discuss physical changes and satisfaction to goals, as well as mental health, sexual health, relationships and intimate part-

Table 5. Effects of Androgenizing Therapy[9,10]

Expected Effects	Potential Adverse Effects
Potentially Permanent • Lower pitch of voice • Enlargement of clitoris • Increased facial and body hair growth • Possible hair loss on scalp ***Typically Reversible*** • Increase in lean muscle mass • Redistribution of fat from hips and buttocks to the abdomen • Cessation of menses • Skin changes, including worsened acne • Increased sex drive • Changes in mood or thinking	• Polycythemia • Potentially irreversible infertility • Pelvic pain and atrophy of vaginal walls, which can increase susceptibility to sexually transmitted infections and pain during penetrative intercourse • Possible increased risk of hyperlipidemia and atherosclerotic cardiovascular disease compared to cisgender women, but likely comparable risk to cisgender men • Increased appetite, weight gain, sweating, increased risk of sleep apnea • Possible increase in irritability/aggression • Teratogen if patient becomes pregnant (birth control recommended if sexually active with partner capable of causing pregnancy)

Table 6. Timeline of Changes After Testosterone Initiation (earliest onset to maximal effect)[9,10]

	1mo	3mo	6mo	1yr	2yr	3yr	4yr	5yr
Oily skin/acne	■	■	■	■	■			
Fat redistribution	■	■	■	■	■	■	■	■
Vaginal atrophy	■	■	■	■	■			
Clitoral enlargement	■	■	■	■	■			
Cessation of menses		■	■					
Facial/body hair growth			■	■	■	■	■	■
Increased muscle mass			■	■	■	■	■	■
Deepening of voice			■	■	■			

Table 7. Testosterone Formulations[9,10]

Formulation/ Administration	Med Name	Dose Frequency	Low Dose	Common Dose	Max Dose	Med Notes
Short-acting injectable *Subcutaneous (typically preferred) or intramuscular*	Testosterone cypionate or enanthate	1-2 weeks (double listed doses if administering biweekly)	25-50 mg	80-100 mg	125 mg	Less frequent dosing leads to higher testosterone level fluctuation. Learning to inject hormones is an additional skill patients must learn.
Transdermal *For all transdermal, avoid skin-skin contact in area of application until completely absorbed.*	Testosterone gel 1% (AndroGel 1%, Testim)	Daily	12.5-25 mg	50 mg	100 mg	1 pump = 12.5 mg Apply to shoulders and upper arms.
Long-acting	TESTOPEL (subcutaneous implantation)	Every 3 months	2 pellets	2-6 pellets	6 pellets	75 mg/pellet: dose range 150-450 mg

ner violence, and pregnancy prevention. Providers should also inquire about the patient's social transition and plans for medical or non-medical gender-affirming treatments.

CONCLUSION

Gender-diverse people experience high levels of discrimination and health disparities, and special attention should be paid to ensuring that clinical environments are affirming for these populations. GAHT can help achieve significant improvement in mental health for gender-diverse patients and is within the purview of primary care providers.

HELPFUL SMARTPHRASES IN EPIC

.ebtransintakemasculinizing
Intake form for patients seeking masculinizing therapy

.ebtransintakefeminizing
Intake form for patients seeking feminizing therapy

.ebconsentfort
Consent form for masculinizing therapy

.ebconsentfore
Consent form for feminizing therapy

.tgncgoalsform
Form for patient to complete with goals for transition

Scan QR code at right for information regarding therapies beyond hormone therapy for gender-diverse persons, as well as definitions for key terms in this article. ➔

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Updates in Neurology

Editor's note: Several advances in Neurology subspecialties in the last 10 years have led to improved patient care. Developments in the fields of neuroinflammation/multiple sclerosis, neuromuscular medicine, vascular neurology, headache medicine, and epilepsy make it important for the non-neurologist to stay abreast. A few advances of which we should all be aware are summarized here by LGHP Neurology providers, who are currently implementing these evidence-based standards of care.

NEW THERAPIES FOR NEUROMYELITIS OPTICA SPECTRUM DISORDER

Wen Y. Helena Wu-Chen, MD, FAAN

Neuromyelitis optica spectrum disorder is an autoimmune disorder characterized by recurrent inflammatory attacks against the astrocyte aquaporin-4 water channel. It primarily affects the optic nerves and spinal cord, resulting in visual deficits and loss of coordination. Although this disorder is rare — affecting 1 to 10 per 100,000 patients — if left undiagnosed and untreated, it can cause blindness and paralysis. Conventional immunosuppressive treatments include rituximab, mycophenolate mofetil, azathioprine, and prednisone, and have been used based on observational clinical studies that lacked masking or control groups.[1,2]

The aquaporin-4 immunoglobin G (IgG) antibody was discovered in the early 2000s and has led to an increased understanding of how the immune system causes astrocyte damage through three crucial targets: the terminal complement system, interleukin-6 (IL-6) receptor, and B cells. Up to 80% of patients have the presence of aquaporin-4 IgG biomarkers.[3]

Because the presence of seropositivity is highly predictive of future relapses, recent treatment efforts have focused on preventive therapies.[3,4]

Recently, randomized controlled trials tested these three therapeutic approaches:

- Among the monoclonal antibodies that inhibit complement component 5 are eculizumab, given every two weeks by infusion, and ravulizumab, given every eight weeks by infusion.

  The primary associated risk is infection by encapsulated organisms such as *Neisseria meningitidis*, therefore a vaccination series must be completed at least two weeks prior to the first dose of antibody treatment.
- Satralizumab, a monoclonal antibody targeting the IL-6 receptor antagonist, is given subcutaneously every four weeks.[3]
- Inebilizumab is a humanized monoclonal antibody that binds to the CD19 surface antigen of B cells, depleting lymphocytes derived from B cell lineage. This is given by infusion every six months.[5]

All patients must be screened for active hepatitis B as well as tuberculosis and cared for appropriately prior to receiving immunotherapy.

NEW EPILEPSY CLASSIFICATION

Heather D. Harle, MD

The International League Against Epilepsy published new guidelines in 2017 regarding definitions/nomenclature of epilepsy subtypes.[6] Terms such as "simple partial" or "complex partial" are often misunderstood and therefore have been updated to be more informative to physicians and patients. The new nomenclature is more descriptive, allowing the care team to understand the different seizure types — a patient may have more than one type — and how they present.

The description outline has three parts: where in the brain seizures begin, the level of awareness during the seizure, and the semiology — that is, the appearance — of the seizure. "Simple partial" has been renamed "focal onset aware," and "complex partial" is now "focal onset impaired awareness."

Finally, whether there is left arm shaking, oral automatisms, feeling of fear, or other presentation is described. If the seizure moves from being focal to generalized tonic clonic, the new term is "focal to bilateral tonic clonic" or FBTCS.

As an example, a patient with seizures of lip smacking and staring would, according to the old system, be identified as having complex partial seizures. According to the new system of classification, we would designate this "focal onset impaired awareness seizure. Semiology: oral automatisms." This gives much more description to all providers so to improve recognition and care.

The terminology has not changed regarding generalized seizures, which are still designated as "tonic clonic," "atonic," or "absence."

AN OVERLOOKED, BUT COMMON MOVEMENT DISORDER

Gabriel Hou, MD, PhD, FAAN

Writer's cramp or hand dystonia is an abnormal unwanted hand muscle spasm that interferes with tasks, especially writing.[7] It may start with a tight grip on the pen. Hand and wrist flexions are more common, with occasional hyperextension of the fingers.[8] Writing is difficult and cannot be sustained; handwriting becomes illegible. Other hand dystonias include typing dystonia or musician's dystonia, which affects playing musical instruments by hand.

A task-specific focal dystonia, hand dystonia is common among patients ages 30 to 50 years old and affects about 15 per 100,000 people.[9] The cause is usually idiopathic. Diagnosis is through clinical history and examinations.

Historically, treatments included anticholinergic medications, which may be helpful for some patients. The newest and most effective treatment includes botulinum toxin injections, which LGHP neurologists now use regularly to target the dystonic carpi and digitorum flexor or extensor muscles. Occupational therapy for sensory and motor skills retuning are also beneficial and considered standard of care.[10]

MULTIPLE SCLEROSIS TREATMENT APPROACH

Neha Safi, MD, MS

Given the many treatment options now available for multiple sclerosis (MS) patients, it can be overwhelming to select which one to initiate first. Previously, clinicians recommended low-efficacy therapies to limit potential side effects and only moved to high-efficacy or escalation therapy if patients manifested breakthrough disease.[11]

Newer studies show that starting high-efficacy therapies in treatment-naïve patients can decrease annualized relapse rates and reduce long-term disability progression.[12] Therefore, choosing anti-CD20 monoclonal antibodies — ocrelizumab or ofatumumab — or an anti-integrin monoclonal antibody such as natalizumab as first-line therapy may be more beneficial in the long run. Insurance companies can be reassured that these first-line therapies are worth the cost to prevent future disability, especially in patients who present with lesions in the posterior fossa or spinal cord.

As patients with MS get older, their immune systems may be less prone to causing new disease activity due to immunosenescence, thus de-escalation or even discontinuation of high-efficacy therapy may be appropriate.[13] The DISCOMS trial was conducted to determine if MS patients age 55 years and older who were stable on disease modifying therapy (DMT) for at least five years could safely discontinue their DMT; it did not demonstrate noninferiority compared to patients who continued on treatment.[14] However, on a case-by-case basis, MS neurologists and their patients may consider stopping DMT if both neurologic exams and MRI scans remain stable and reassuring.[15]

UPDATES IN MYASTHENIA GRAVIS

Allison Crowell, MD

Myasthenia gravis is a disorder of neuromuscular junction transmission that affects approximately 14 to 20 per 100,000 people, accounting for roughly 350,000 to 600,000 cases in the United States. Although it is a relatively rare condition, advances in targeted therapeutic interventions have changed the way that neurologists treat patients with myasthenia gravis in recent years.

In patients with myasthenia gravis, complement inhibition at the neuromuscular junction can result in more acetylcholine receptors at the post-synaptic junction, improving neuromuscular junction transmission and muscle contraction.

New classes of medications include complement inhibitors, such as ravulizumab and zilucoplan. Risks of complement inhibition include infection such as meningococcal meningitis. Vaccination is required prior to the initiation of treatment.

A second class of novel treatments includes the neonatal Fc receptor (FcRn) monoclonal antibodies efgartigimod and rozanolixizumab. Autoantibodies against IgG bind to the FcRn and reduce the amount of circulating pathogenic IgG antibodies, including those that attack the neuromuscular junction in myasthenia. The overall reduction in IgG antibodies does increase the risk of upper respiratory tract and urinary tract infections.

Both of these new classes of medications result in immunomodulatory, rather than immunosuppressive, effects; therefore treatment-related adverse effects are mild to moderate and do not result in significant immune compromise.[16-18] The price of these new medications is high, but assistance programs and insurance approvals are not challenging to navigate.

UPDATES IN HEADACHE NEUROLOGY

Ellen Michelle Gibson Depoy, MD

Migraine remains a major reason for absenteeism from work and school. The past decade has witnessed robust innovation of novel drug classes. These include calcitonin gene-related peptide (CGRP) antagonist monoclonal antibodies and small molecule CGRP antagonists (gepants), the latter of which are available as oral medication and have a shorter half-life.

CGRP is a 37-amino acid neuropeptide present in the peripheral and central nervous systems that has been shown to ignite the migraine signaling pathway.[19,20] CGRP-targeting therapies were specifically developed for migraine treatment, and several randomized clinical trials demonstrate efficacy and tolerability compared to both placebo and off-label migraine preventive medications, i.e., beta blockers, antiepileptic medications, and antidepressants.

The efficacy of CGRP antagonists in preventive treatment, paired with excellent safety and tolerability profiles, has revolutionized headache treatment. Specifically, these therapies do not seem to cause liver problems and are not associated with medication-overuse headache — two issues that must be faced with more classical agents.

American Headache Society guidelines state that CGRP antagonists are first-line therapies for migraine prevention, based on efficacy, safety, and tolerability data from several randomized clinical trials.[21] A significant downside includes the high cost of CGRP antagonist medications, and this may continue to be a concern until generic formulations are available.

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PEARLS OF EDUCATION

Treating Behavioral Health in the Pediatric Population

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Editor's note: The following article offers insights and practice guidelines from the Pediatric Behavioral Health Conference, hosted by Penn Medicine Lancaster General Health in November 2023. Full recordings of conference sessions are available online; access the recordings at LGHealth.org/CME via the "CME On Demand" link.

INTRODUCTION

The mental health crisis in the pediatric population remains a growing concern. Unfortunately, there are not enough psychiatric providers to meet the increasing demand. Therefore, all pediatric primary care providers (PCPs) should have the ability to diagnose and manage psychiatric conditions either independently or until the patient establishes care with Psychiatry.

The goal of the 2023 LG Health Pediatric Behavioral Health conference was to teach PCPs to recognize, screen, and treat common psychiatric conditions to improve the mental health of the community. The conference reviewed some of the most common mental health disorders, including depression, anxiety, suicide, attention-deficit/hyperactivity disorder (ADHD), and their appropriate treatments.

Begin by clarifying the balance between confidentiality and safety: "I value your confidentiality, but as a medical provider it's my obligation to disclose any safety concerns that come up during our discussions. Do you have any questions about that?"

Suicidal Ideation and Action in the Primary Care Office

Presentation by Sarah Arshad, MD

In 2020, after unintentional injury, suicide was the second leading cause of death in children ages 10-14. Ten percent of high school students report making a suicide attempt. Suicidal ideations range from passive thoughts of death to active thoughts with intent that can lead to suicidal acts.

Risk factors for suicide include previous suicide attempts, mental health conditions, substance use, poor interpersonal relationships, barriers to health care, stigma, and socioeconomic factors. Protective factors include good coping skills, supportive relationships with adults, access to health care, and limited access to lethal means.

The first step to evaluation is screening. Per American Academy of Pediatrics recommendations, screen children ages 8 to 11 years when clinically indicated and universally at age 12, and screen patients under age 8 if they show warning signs or if there is parental concern. The screening process should be structured using a standardized screening tool such as the Columbia Suicide Severity Rating Scale (C-SSR), but relying solely on these has the potential to miss high-risk patients. Information obtained through screening should be used in conjunction with collateral history from patients, guardians, and your clinical assessment.

Begin the process by clarifying the balance between confidentiality and safety. One way to introduce this to patients is to say, "I value your confidentiality, but as a medical provider it's my obligation to disclose any safety concerns that come up during our discussions. Do you have any questions about that?" Next, establish rapport by using open-ended and non-threatening questions. Identify the patient's position on the spectrum, then clarify means/access and plan, especially if they have active thoughts.

Questions about thoughts of suicide, suicidal plans, and prior suicide attempts should follow. It can be helpful to normalize behaviors, for example, "Sometimes when teens are depressed, they have thoughts wishing they were dead or about killing themselves. Have you ever had those thoughts?" Patients with adequate means and detailed plans are at greatest risk of suicide.

Additionally, ask about suicidal behaviors in preparation for the attempt that should raise your level of concern. Examples of such behaviors include gathering harmful supplies or doing a "walk through" of a

bridge or building. Patients with a negative screen should be equipped with tools on how to seek help when needed. Patients with a positive screen need further risk stratification to determine if they require urgent referral to emergency services (see Fig. 1).

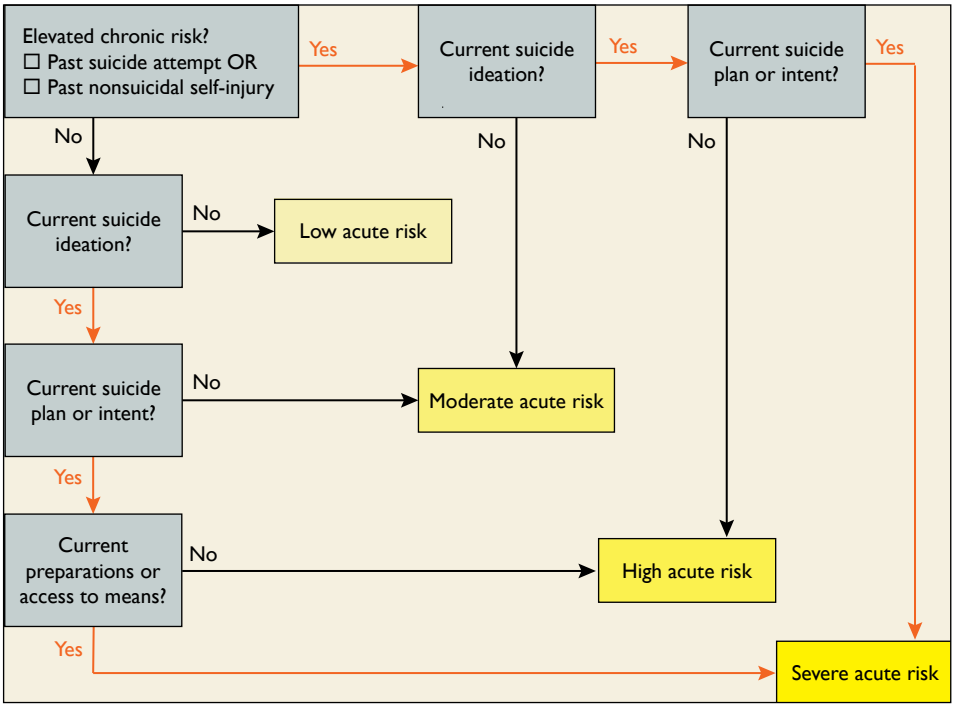

Fig. 1. Suicide risk algorithm, offered to help providers assess a pediatric patient's risk of suicide.[1]

Safety planning is the next step, once risk level is determined. Suicide risk fluctuates over time; safety planning equips children and teens with ways to respond to emotional crisis that could occur in the future. It should include cognitive behavioral approaches and tools regarding how to reach out to appropriate adults during the crisis. The goal is to prevent a suicide attempt. A good safety plan should include:

1. Identify warning signs of a crisis — these are child-dependent and may include irritability or hiding in their room.
2. Share coping skills and accessible tools to use during a crisis — for example, distraction, relaxation, talking to someone, or playing with pets.
3. Generate a list of trusted adults (older than 18 years old) in different environments that they can share depressive and suicidal thoughts with. Adults should be reachable by different modalities (text, phone).
4. Ensure safety of the environment by keeping harmful things away from the patient. This includes locking up medications and securing sharp objects. Firearms should be locked separately from ammunition.

Tailor a safety plan to each child's needs. It is acceptable to exclude components if they are not beneficial to the child. If possible, involve a trusted adult or guardian when creating the safety plan.

An example of a good safety plan is the Stanley-Brown plan, available online. To review, scan the QR code at left or visit sprc.org/online-library/stanley-brown-safety-plan/

Q&A on Advanced/Complex ADHD

Panel discussion by Sarah Arshad, MD; Consuelo Cagande, MD; and Ty Bristol, MD, MPH

How do you differentiate ADHD from comorbid conditions? Diagnosing pediatric ADHD is a complex process, especially in children ages 6 years or younger, because ADHD can occur comorbidly with other psychiatric disorders. It is imperative to give the correct diagnosis prior to initiating treatment. Some tips on how to approach this include:

- Rule out language barriers and developmental milestone delays.
- Use more than one screening tool to help tease out the predominant symptoms and differentiate from anxiety and autism. For example, anxiety tends to present with mood symptoms. ADHD typically presents early in life compared to anxiety, which tends to occur in school-aged kids.
- Inquire about the child's social environment and family structures.
- Try behavioral therapies and parent management training prior to pharmacotherapy.
- Focus first on treating symptoms that cause the most impairment.

What are the recommendations on medical marijuana for ADHD treatment? This is not recommended, as there are no studies or evidence of efficacy in pediatric patients.

More is known about the negative side effects, including increased impulsivity, increased risk of substance use disorders later in life, and poor neuro-circuitry formation. Also, some evidence links psychosis and depression to chronic marijuana use in children. Patients and their parents need appropriate education about the potential risks of using marijuana. Children and teens with untreated ADHD are at higher risk of substance use disorder, dropping out of school, and "getting associated with the wrong crowd."

What about ADHD in patients with known substance use disorder? First treat the substance use disorder by getting patients into recovery. Once they are drug free, PCPs can address ADHD and mood disorders. For ADHD, use long-acting stimulant medications or a non-stimulant, like atomoxetine, with low abuse potential.

Are generics as efficacious as name brand? Sometimes. If limited by insurance, it is acceptable to trial generics first; assess efficacy, and then titrate or modify as needed. Consider a switch to brand-name medication to achieve maximum therapeutic effect. Lexicomp and UpToDate offer good tables to reference when converting between stimulant medications.

Is it worthwhile to use non-stimulant medications as first line? Yes, in certain patients. Although non-stimulants such as alpha-agonists and atomoxetine are not as effective, it is acceptable to trial them first, especially in children younger than 4 years or per parent preference.

What about insomnia in patients with ADHD? Screen all patients for sleep disorders when evaluating for ADHD. Good sleep is important in ADHD. The first step for treatment of insomnia is behavioral modifications for the child and often for the parents as well. Unfortunately, there is no pharmacologic treatment for sleep in children approved by the Food and Drug Administration (FDA). Up to 10 mg of melatonin can be used as a sleep aid in patients that do not respond to behavioral changes.

Is it possible for a medication to stop working? Yes. Patients may need to switch back and forth between medications or need dose adjustments after years of stability on a particular dose. The pathophysiology behind this is unknown at this time.

Is there a role for genetic testing in determining treatment? Only to a very limited extent. Tests such as Gene Sight® can be used to describe how a specific person metabolizes medications, but it does not elucidate which medications to use.

Is there a link between lead poisoning and ADHD? Yes, heavy metal poisoning can increase the risk of ADHD and other neuropsychiatric disorders.

What do you do if a patient develops tics after initiating stimulant therapy? Stimulants do not cause tics but can unmask an underlying tic disorder. Tics are frequently caused by anxiety. Start treatment with behavioral therapy, then consider an alpha-agonist or atypical antipsychotic for severe cases. Consider referral to a pediatric neurologist or child psychiatrist if tics persist.

Are electrocardiograms (EKGs) necessary to start stimulants? No. The American Heart Association does not recommend routine baseline EKGs before starting stimulants. If there is a family or personal history of cardiac issues or if a child is on medications that can prolong corrected QT interval (QTc), then an EKG or cardiologist referral is appropriate.

Advanced Anxiety

Presentation by Consuelo Cagande, MD

The pediatric anxiety disorder triad includes separation anxiety, generalized anxiety, and social anxiety disorder. These disorders are common, present similarly, and can be difficult to distinguish from each other. Suspect an underlying anxiety disorder in children with sleep or eating problems, excessive need for reassurance, explosive outbursts, poor performance at school, and avoidance of interpersonal activities.

Table 1. **Reuptake Inhibitors**

Medication	FDA-Approved Indication; Age	Typical Dose Range	Typical Starting Dose	Typical Titration Increments	Max Daily Dose	Common Adverse Effects
First-Line Selective Serotonin Reuptake Inhibitors (SSRIs)						
Sertraline (Zoloft™)	OCD; ≥6 years	Children 25-100 mg Adolescents 50-150 mg	12.5-25 mg daily	12.5-25 mg for doses <50 mg 25 mg for doses >50 mg	200 mg	GI upset, headache, insomnia
Fluoxetine (Prozac™)	MDD, OCD; ≥8 years	Children 5-10 mg Adolescents 10-40 mg	5-10 mg daily	5 mg for doses <20 mg 10 mg for doses >20 mg	60 mg	Nausea, headache, weight reduction, abdominal pain
Second-Line Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) — if failed trial of both SSRIs						
Duloxetine (Cymbalta™)	GAD; ≥7 years	Children, adolescents 30-60 mg	20-30 mg daily	20-30 mg	120 mg	Nausea, headache, weight reduction, abdominal pain

Children can also present with "midline physical symptoms," which include headaches, dizziness, swallowing issues, shortness of breath or hyperventilation, chest or abdominal pain, bowel or bladder urgency, and tingling in fingertips. Consider anxiety if three or more physical symptoms persist after ruling out all possible metabolic causes.

Age of onset is typically around 6-12 years, so screening should be done as soon as symptoms appear. Begin evaluation by inquiring about recent life events, adverse childhood experiences, social determinants of health, family history, and gender and sexual identity. Also tease out comorbidities, including depression/suicidal ideation, trauma, and disruptive behaviors. Commonly used screening tools are the Screen for Child Anxiety Related Disorders (SCARED) form, which has child and parent versions, and the Generalized Anxiety Disorder-7 (GAD-7) scale, which is more useful for children ages 13 and older.

First-line treatment is cognitive behavioral therapy, mindfulness-based psychotherapy (especially in social anxiety disorders), and selective serotonin reuptake inhibitors (SSRIs) (see Table 1 on page 85). Maximum benefit is achieved with a combination of psychotherapy and SSRIs. Avoid benzodiazepines or antihistamines for anxiety. Consider atomoxetine in children who have comorbid ADHD.

"SSRIs: Things I Learned Transitioning from PCP to Psychiatrist"

Presentation by Tyrone Bristol, MD, MPH

Medications should be used in conjunction with behavioral therapies. SSRIs are the first-line pharmacologic treatment for pediatric anxiety and depression. They result in fewer side effects than tricyclic antidepressants and monoamine oxidase inhibitors, and they are safer in overdose. All SSRIs are equally effective and have been FDA approved for multiple indications in addition to depression and anxiety, including obsessive-compulsive disorder (OCD) and OCD-spectrum disorders, bulimia and anorexia nervosa, and premenstrual dysphoric disorder (see Table 2).

The SSRI choice is based on the patient's response and patient-specific side effect profile. Be cautious of drug-drug interactions prior to initiating SSRI therapy. Since they are metabolized by the liver cytochrome P450 enzymes, they can lead to increased or decreased effectiveness of certain medications, e.g., oral contraceptive pills. Also, avoid concurrent use with other serotonin-containing medications. You should expect symptom improvement after one month of therapy, so we recommend switching to an alternate SSRI if there is zero improvement. About 50% of patients who fail one SSRI will respond positively to a different one.

Start with low doses, titrate up slowly but not too slow (see Table 3). In severe cases, increase doses weekly to achieve typical dose. Children and adolescents may need higher doses to achieve therapeutic effect. If a second SSRI is not helpful, then switch to a serotonin-norepinephrine reuptake inhibitor (SNRI).

Monitor for side effects. Sexual dysfunction is the most common side effect but is seen more in adult patients. Other side effects are headaches (seen mostly with fluoxetine), gastrointestinal (GI) side effects and weight loss (paroxetine has been shown to cause more pronounced weight gain compared with other SSRIs), QTc prolongation (especially with citalopram), insomnia, anxiety, restless legs, and emotional blunting.

There is a risk of serotonin syndrome if taken simultaneously with other serotonin-containing medications or supplements (e.g., St. John's Wort). Withdrawal symptoms can occur with abrupt discontinuation. Counsel patients about possible side effects prior to initiating treatment.

Table 2. FDA-Approved Medications That Can Be Used for Children and Teenagers[2]

Medication *Recommended initial dose and maximum dose vary by age*	**Approved for Patients Ages ...**
Clomipramine	10 years and older who have obsessive compulsive disorder
Duloxetine	7 years and older who have generalized anxiety disorder
Escitalopram	12 years and older who have major depressive disorder
Fluoxetine	8 years and older who have major depressive disorder
Fluoxetine	7 years and older who have obsessive compulsive disorder
Fluvoxamine	8 years and older who have obsessive compulsive disorder
Lurasidone	10 years and older who have bipolar depression
Olanzapine and fluoxetine, combination drug	10 years and older who have bipolar depression
Sertraline	6 years and older who have obsessive compulsive disorder

Regarding SSRI use in pregnancy, avoid paroxetine use due to increased risk of congenital heart defects and discontinuation syndrome in newborns. Also, paroxetine and sertraline can cause persistent pulmonary hypertension in newborns. A small amount of SSRI passes into breast milk, but there are

no known harmful effects to breastfed infants. Sertraline and escitalopram have lower concentrations in breast milk compared to fluoxetine.

Self-Care While Taking Care of Mental Health Patients

Presentation by Sarah Arshad, MD

Dealing with mental health issues can be challenging. Providers frequently have high expectations for success, and when they do not meet them, it can lead them to feel bad about themselves. Self-care is important and should be personalized.

- **Challenge:** You as the health care provider feel like you are not doing enough. Example: patient is not responding as expected or patient is refusing treatment.
  Reframe: Psychiatric disorders are chronic syndromes that may not improve immediately. Small steps in the right direction are a win; create long-term goals. Your role is as a guide to your patients; it is not to fix all the problems. You are not in control of what your patient does outside of the office.
- **Challenge:** Demanding patient. Example: new patient requested to be started on stimulant prior to adequate assessment from you.
  Reframe: Do your best to be empathic and acknowledge their concerns. Establish boundaries within your reasonable ability.
- **Challenge:** Demanding families. Example: family frustrated by systemic issues but directing frustration at you.
  Reframe: Address concerns without taking on blame: Connect patients to services that may help. Advocate for change within your own system. You do not have the ability to fix everything.

Other Tips

- Take a break (step out of the room for five minutes, take deep breaths, collect your thoughts).
- Reach out to colleagues for support.
- Engage in self-care and relaxation strategies that work for you. What "fills your cup"?
- Accept that it is okay to give the case to a colleague if the patient or situation continues to be a challenge.
- Give yourself grace.
- Utilize current resources at hand.

CONCLUSION

Managing pediatric mental health conditions can be a challenge with opportunities for success. Start by using the appropriate assessment tool to screen for the suspected condition. Remember that neuropsychiatric disorders can occur comorbidly, so focus on treating the symptoms that cause the most impairment first.

Always consider behavioral therapy for the child, and occasionally the parents as well, as the first step of your treatment plan. Start low and go slow when initiating pharmacotherapy, but remember that children and adolescents often need higher doses to achieve therapeutic effects. Use your colleagues as a resource and support system, and take care of yourself so you can continue taking care of your patients.

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Table 3. SSRI Dosing and Timing

Medication	Available Forms	Starting Dose	Timing	Med Notes
Sertraline	Scored tablet, liquid	12.5-25 mg daily	Every morning or every night at bedtime	• Take with food to minimize GI side effects.
Fluoxetine	Capsule, scored tablet, liquid	5-10 mg daily	Every morning, due to risk of anxiety and insomnia	• Switch to nighttime if increased sleepiness. • Take with food to minimize GI side effects. • Consider every-other-day dosing to mitigate side effects.
Escitalopram *Approved May 2023 for GAD*	Scored tablet, liquid	10 mg daily, max 20 mg	Every morning or every night at bedtime	• Sedation properties may help with insomnia. • Avoid use in patients with severe symptoms due to low maximum dose.
Fluvoxamine	Scored or unscored tablet	25 mg daily	Every night at bedtime	• Only SSRI not approved by FDA as an antidepressant. • Slow titration to avoid GI effects. • Consider twice-a-day dosing due to short half-life.

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NARRATIVE MEDICINE

Nerve Pain

Jon Lepley, DO, FAOAAM
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Penn Medicine Lancaster General Health

Lisa was a real thorn in my side as a patient in the Philadelphia jail 10 years ago. She was a twentysomething-year-old, mostly healthy female who somehow entered my chronic medical care clinic within a day of entering the jail. Urgent appointments in the chronic care clinic were typically reserved for someone with insulin-dependent diabetes or severe asthma. Lisa was placed on my schedule for "nerve pain."

Although all detainees met with a nurse within four hours of entering the jail to identify urgent problems and continue existing medications, physician evaluations for chronic illnesses were routinely scheduled to occur three weeks after a person entered the jail. This timeframe provided a crucial advantage. The jail system routinely processed more than 30,000 people a year,[1] but at least half were released within two weeks. Seeing every incarcerated person with a health problem before then was unfeasible.

Sometimes, persistence trumped procedure at the jail in the face of vociferous patients, no matter how minor the complaint. Bearing prominent and protruding brown eyes against a gaunt face — I initially wondered if she had a thyroid problem — Lisa confidently strode into the exam room. She offered to make the appointment easy for me.

She said, "You just need to prescribe me Pamelor, and then after I try that for four weeks, I will come back, and you can give me my Neurontin."

I was the one who prolonged the interaction by asking where she had pain, for how long, and how the problem was initially diagnosed. She helpfully pointed out that I had many patients to see and could get on to more meaningful work by following her lead and prescribing a low dose of nortriptyline.

A noticeable cacophony of gripes from many older patients outside the exam room door waiting to see me validated Lisa's observation. I was swamped and obliged, hoping she would follow the probabilities and leave within two weeks. The odds did not play out that way.

Lisa returned to my clinic after four weeks with a chief complaint of "nerve pain." Her eyes were less prominent, and her face was fuller. She was wearing makeup crafted from soft drink mix and powdered sugar. The ever-present low rumble from older patients with medical concerns waiting outside the exam room door continued to make me feel rushed.

Lisa again took charge of the interaction, pointing to a filing cabinet in the corner of the exam room. "Just fill out the paper in that drawer saying Pamelor did not work so you can give me my Neurontin, " she directed.

Indeed, the filing cabinet did contain a form for non-formulary requests. Formularies are standard in correctional health, just like in community health settings. However, some inexpensive medications are non-formulary because they are problematic in other ways. A prescription for gabapentin for "nerve pain" — especially from the new jail doctor — would likely elicit hundreds of requests from other patients with the same complaint.

This time, I pushed back. I pointed out that I had prescriptive authority despite her propensity to call it *her* Neurontin. I remarked that she did not appear very ill, and the many people grumbling — now more loudly and impatiently — outside the exam room door had needs that outweighed this unsubstantiated complaint of "nerve pain."

This did not deter Lisa; she persisted until I eventually completed a non-formulary request for gabapentin. Over subsequent weeks, my efforts to stick to a relatively low dose were futile. I eventually increased her gabapentin prescription to 800 mg three times per day, which fulfilled another one of Lisa's prophecies: "That is the only dose that will work for me."

Yet, that did not eliminate her presence in my chronic care clinic. Lisa was an ever-present force on my schedule in the months that followed.

She complained about the fish served for dinner every Friday and requested a note from me stating that

she needed an alternative. She also wanted a note saying that a bottom bunk was medically necessary and that she needed two mattresses. Only having one mattress was terrible for her back, she said, and might exacerbate her nerve pain. Without that note, she might need tramadol.

The implicit threat of a campaign for tramadol (also non-formulary for reasons other than the cost) was not benign. Time was a crucial resource, and Lisa tended to linger in the exam room longer than necessary after achieving her day's objective. I usually spent that time laboriously describing the difference between medical and humanitarian problems and reminding her that my job was only to address one of those categories.

Yet, such exchanges were not always bitter. After one somewhat playful debate about whether combining two thin, hard mattresses would provide comfort equal to a well-crafted soft one, Lisa peered suspiciously at me while I wrote in her chart.

"What are you writing about me?" she asked.

"I am simply preparing for the eventual deposition," I responded in exasperation and only half-jokingly. Lawsuits were widespread in the Philadelphia jail.[1]

"I wouldn't sue you," she reassured me. "You are a nice doctor." Compliments did not come easily at the jail. On that day, I needed one. The jail was a difficult place for both of us.

At security orientation for the job, correctional officers warned me about the unscrupulous nature of inmates and the importance of always keeping them at arm's length. The training was brought to life with striking examples of weapons crafted by prisoners from seemingly harmless everyday items like soap, toothbrushes, and toilet paper.

However, cautionary tales involving prisoners who manipulated staff to undermine rules in the institution — sometimes called "getting got"[2] — fixed more deeply in my mind. In extreme cases, staff unwittingly facilitated an escape or introduction of dangerous contraband into the inmate population. These relationships gone awry seemed to have a partial foundation in empathy and human connection toward the incarcerated individual.

I guarded against this phenomenon carefully. Patients who attempted to direct their medical care — a natural inclination protected by the pillar of autonomy — provoked suspicion. Praise from patients may not have been genuine; rather, it could have been a Machiavellian effort to subvert a system designed to reform them. Detachment had its value in avoiding this can of worms altogether.

Such disconnection was not my natural inclination and required work. That day, perhaps more tired and beleaguered than usual, I received Lisa's compliment with gratitude. With a less guarded demeanor, I saw beyond her uniform of jailhouse makeup and blue jumpsuit, and I became curious about Lisa's life outside the jail. I wondered if she had children and an occupation. I imagined her as an overprotective parent, a fearsome litigator, or a highly effective salesperson.

Lisa's primary care provider outside the jail undoubtedly knew these aspects of her life. I avoided discovering them for fear of a perceived slippery slope without considering a more precipitous descent that accompanied purposeful disconnection. Over time, I discovered that an ideal middle ground lay someplace in between — a precarious peak requiring constant balance to avoid sliding too far into an abyss on either side.

Yet, I did not learn much more about Lisa because, as is always the case, her time at the Philadelphia jail was limited. Patients were eventually transferred to a state correctional institute for a longer sentence or went home.

Lisa went home, but not for long. I learned that she died of an opioid overdose the day after she was released.

Among her countless petitions, one thing Lisa never requested was buprenorphine for opioid use disorder. Such a request would have been reasonable and lifesaving if met[3] because Lisa was regularly injecting heroin before entering the jail. Yet, many prior instances of incarceration taught her that this request was outside the realm of negotiation.

Lisa's assumption 10 years ago was correct. I routinely denied such requests despite regularly prescribing buprenorphine in the community up to that point. Denying access to that medication was the status quo among all health care providers working at the jail, and conformity was comfortable. Within a milieu that cultivated patient mistrust, it was not difficult for me to rationalize that prisoners who requested buprenorphine were trying to maintain addiction instead of freeing themselves from it.

Lisa, and hundreds like her, managed opioid cravings by requesting sedatives like gabapentin and other minor comforts from me instead. The prevalent complaint of "nerve pain" throughout the jail was not just

a premise for receiving these tokens; it was a stand-in for more profound discomfort caused by many intractable, unsolvable problems.

Psychoactive medications offered temporary anesthesia, as did genuine human interaction with the jail doctor — however contentious at times.

Nowadays, I do not work in a jail but in a family medicine office, and every patient I meet who displays a clinical need for buprenorphine promptly receives a prescription. Equally important, I warmly accept patients' compliments when offered; I may even place a hand on their shoulder if that is helpful during trying times. When I prescribe medication to treat addiction and cultivate a therapeutic alliance, I think about Lisa and others left behind.

Fatal overdoses trigger a cascade of interminable pain that ripples through family and friends. A dissection of the event will reveal many systemic problems, frequently involving overpopulated jails, prisons, and community probation and parole.[4] Health care providers working in these overburdened systems may experience a different but equally valid ache.

We may have been conditioned to view patients as adversaries. We may have been compelled to withhold or withdraw lifesaving medication that can prevent fatal overdose. We may be plagued by deep regret for perpetrating, failing to prevent, or bearing witness to circumstances that violate our moral code.[5]

Academics label this phenomenon moral injury. I describe it as nerve pain.

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PHOTO QUIZ FROM URGENT CARE

Mastoiditis

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CASE HISTORY

A 3-year-old female presents on a Friday afternoon with left ear redness and persistent pain for the last four days. The patient's mother — the main source of history — states that the child has been having fevers since Tuesday, with the highest recorded temperature of 104˚F this morning.

The patient has had decreased appetite and fatigue for the past 48 hours. The patient has no known allergies. A chart review shows one prior episode of uncomplicated otitis media.

Regarding the ear, there has been no drainage, change in hearing, tinnitus, bleeding, or dizziness. The mother noticed swelling and redness behind the left ear yesterday afternoon.

The mother has been giving the patient Tylenol or Motrin to help control the fever and pain.

The vital signs are normal at the time of the clinic visit. On exam, there is erythema behind the ear (see Fig. 1). Further exam shows bulging and erythematous tympanic membrane with no serous fluid present. The middle ear ossicles cannot be visualized.

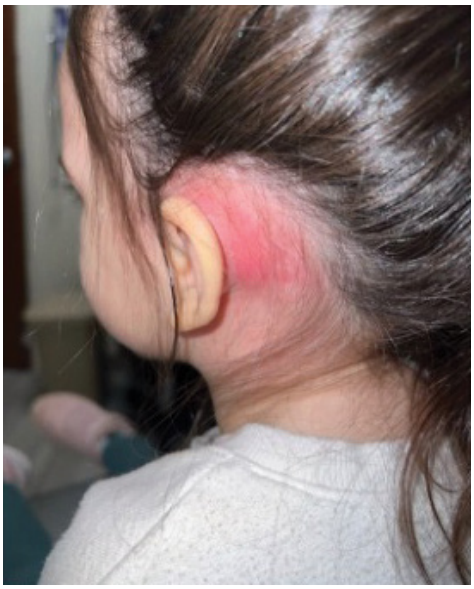

Fig. 1. Photo of patient's left ear taken by provider in urgent care setting.

QUESTIONS

1. What are the symptoms and signs of mastoiditis?
2. Who is at risk of mastoiditis?
3. What are the most common microbial pathogens in mastoiditis?
4. What is the relationship between acute otitis media and mastoiditis?
5. Which lab tests are used in the workup of suspected mastoiditis in a patient?
6. What are complications of mastoiditis if not treated properly?

ANSWERS

1. Symptoms of mastoiditis include pain behind the ear and fever, which can make the patient uncomfortable. Signs of infection include erythematous skin overlying the mastoid area and proptosis of the auricle. Tenderness and inflammation over the mastoid process are signs of a potentially surgical mastoiditis.
2. Most children that present with acute surgical mastoiditis are younger than 2 years of age and do not have history of frequent otitis media.
3. The most common pathogens in mastoiditis are *Streptococcus pyogenes, Streptococcus pneumonia, group A beta-hemolytic streptococci, Staphylococcus aureus, Moraxella catarrhalis,* and *Haemophilus influenzae.*
4. In some patients with acute otitis media, the infection can spread beyond the mucosa of the middle ear cleft to develop osteitis within the mastoid air cell system or periostitis of the mastoid process. This process can be caused either through direct bone erosion or indirectly by the emissary vein of the mastoid.
5. Labs tests and other testing might include:
   a. A complete blood count and sedimentation rate to establish baseline; these can be used to evaluate the efficacy of therapy.
   b. A tympanocentesis or myringotomy to obtain a bacterial culture.
   c. Audiometry, performed after convalescence

from the acute phase and with children who have chronic mastoiditis. However, in the at-risk population (children <2 years of age), thresholds for air and bone conduction under headphones are not well established.

d. A CT scan of the temporal bone if CT scanning is not immediately available; plain radiographs of the mastoids often demonstrate clouding of the air cells with bone destruction.

6. Complications of improperly treated mastoiditis can include: permanent hearing loss, facial nerve palsy, cranial nerve involvement, osteomyelitis, petrositis, labyrinthitis, Gradenigo's syndrome, intracranial extension (meningitis, cerebral abscess, epidural abscess, subdural empyema), sigmoid sinus thrombosis, and abscess formation.

DISCUSSION

Mastoiditis is a suppurative infection of the mastoid air cells with typical symptoms of less than one month's duration. Cases may vary from uncomplicated to complicated; the latter involves one or more extra- or intracranial complications. It is known to be the most common intratemporal complication of acute otitis media.[1]

The most common bacterial species implicated are *Streptococcus pyogenes* and *Streptococcus pneumoniae.* Less common bacterial species include *Haemophilus influenza, Staphylococcus aureus* including MRSA, and *Pseudomonas aeruginosa.*

The most common risk factors are recent ear infection and young age, typically less than 2 years old. Associated findings include high fever, as well as high white blood count, absolute neutrophil count, and inflammatory markers. Less significant risk factors are previous antibiotic therapy or no history of previous middle ear infections.[2] Consultation with an otolaryngologist should occur early in the disease course.

A computed tomography with intravenous (IV) contrast of the temporal bone is the standard for evaluation of mastoiditis, with sensitivities ranging from 87% to 100%.[3] There is variability in practice style, but children with intracranial abnormalities such as abscess are more likely to undergo aspiration and drainage.[4]

Mastoiditis may be treated initially with conservative management before considering surgical intervention. Initial treatment should consist of IV antibiotic therapy and middle ear drainage with myringotomy with or without placement of a tympanostomy tube.[3] Most children with uncomplicated acute or subacute mastoiditis can be managed without mastoidectomy; however, patients should be monitored daily for clinical response, and simple mastoidectomy should be performed if there is no clinical improvement in systemic and local findings within 48 hours.[1]

Acute mastoiditis can be complicated by isolated facial nerve paralysis, which can initially be managed conservatively. Other complications may include subperiosteal abscess, Bezold's abscess, osteomyelitis involving other parts of the skull, labyrinthitis, meningitis, subdural abscess, epidural abscess, brain abscess, cerebellar abscess, or septic dural sinus thrombosis.[5]

Patients with suppurative extracranial or intracranial complications of acute mastoiditis other than facial nerve paralysis are candidates for aggressive surgical management with mastoidectomy, in addition to IV antimicrobial therapy and myringotomy.[3] Patients should follow-up with an otolaryngologist within two weeks after symptoms resolve.

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SPOTLIGHT ON CLINICAL RESEARCH

DCM-DETECT

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Madara

Editor's note: This is the 20th in a series of articles from the Penn Medicine Lancaster General Health Research Institute that describes ongoing research studies. Members of the LG Health staff who are conducting research and wish to have their studies described here are encouraged to contact the offices of JLGH *at 717-544-8004.*

The "Dilated Cardiomyopathy Detection using AI and screening with mobile Technology (DCM-DETECT)" protocol is an LG Health von Hess Grant funded study that aims to utilize artificial intelligence (AI) to analyze EKGs to screen for dilated cardiomyopathies.

Studies have shown that 10% to 20% of patients with a non-ischemic dilated cardiomyopathy (DCM) have an identifiable genetic etiology. Current American Heart Association and American College of Cardiology recommendations are that all their first-degree relatives (FDRs) undergo a screening echocardiogram to detect asymptomatic left ventricular dysfunction. Due to costs and logistical concerns, compliance with these recommendations is low even though current therapy for DCM is effective and potentially life altering.

In the DCM-DETECT study, each proband — the first family member identified with a non-ischemic DCM — will be recruited and asked to:

- Provide demographic information and family medical history.
- Complete a 6-Lead EKG using a mobile EKG device.
- Contact their FDRs to invite them to join the study.
- Encourage their FDRs to obtain cardiac screening by echocardiogram.

FDRs who choose to participate will also complete the mobile 6-Lead EKG and survey. In addition, they will be encouraged to obtain an echocardiogram through their health care provider. The primary objective of the study is to assess the impact of screening FDRs of patients with DCM using the mobile EKG device. The primary endpoint of the study will be measured by the subsequent uptake of cardiac screening in FDRs.

The study team is utilizing a mobile EKG device developed by AliveCor to show the applicability of screening tools incorporating AI technology to the general population. The Mayo Clinic has developed an FDA-approved algorithm that uses cloud-based AI to analyze the EKG recordings. This algorithm can detect an impaired ejection fraction with a high degree of sensitivity and specificity. The study will compare the AI-analyzed EKGs to echocardiogram results in both screen-positive and screen-negative participants.

Study participants will also include a cohort of Amish and old order Mennonite patients recruited from the Central Pennsylvania Clinic to clarify the barriers to care in this medically underserved population who have an elevated incidence of genetic cardiomyopathies.

This study is being done in parallel with the Mayo Clinic, Rochester. Data collection and analysis will be local, and the results will be pooled at the completion of the study at all sites. The enrollment goal at LG Health is to recruit 50 probands from The Heart Group (THG) and five from the Central Pennsylvania Clinic. We aim to further enroll approximately 120 FDRs of the probands from these two sites.

The principal investigator of this study at LG Health is Roy Small, MD (THG Advanced Heart Failure Clinic and Medical Director, Penn Medicine LG Health Research Institute). D. Holmes Morton, MD (Central Pennsylvania Clinic), Tareck Nossuli, MD, PhD (THG Advanced Heart Failure Clinic), and Douglas Gohn, MD (THG Electrophysiology) are co-investigators.

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TOP TIPS FROM FAMILY PRACTICE

Cervical Cancer, Anaphylaxis, ACLS, Breast Cancer Screening

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CERVICAL CANCER SCREENING BEST PRACTICES[1]

Although the American Cancer Society (ACS) in 2020 updated its cervical screening guidelines, proposing two major changes — start cervical cancer screening at age 25 rather than age 21, and perform primary human papillomavirus (HPV) testing instead of a pap test — a survey published earlier this year found few clinicians actually follow these recommendations. The reasons cited are multifaceted.

First, health care providers in the United States may be unsure how to reconcile conflicting cervical cancer screening guidelines from another major organization — the U.S. Preventive Services Task Force (USPSTF), which published guidelines in 2018. Although the ACS guidelines are based on an analysis of the latest evidence, their recommendations challenge those from the USPSTF, which dictates insurance coverage in the United States.

Last year the America College of Obstetricians and Gynecologists (ACOG) aligned its guidelines with those from the USPSTF, which recommends average-risk individuals start pap testing, not HPV testing, at age 21, and broadens the options to primary HPV testing, pap testing, or both together starting at age 30. ACS, on the other hand, says primary HPV testing is the preferred screening approach from the start — that is, at age 25.

Because the ACS guidelines marked a notable departure from prevailing practice, a team of researchers from five U.S. universities sought to find out if anyone was following them. The results, published in the journal *Cancer* in March of this year, revealed that most health care providers had not changed practice.[2]

One professor of obstetrics and gynecology at Boston University commented, "It's really just a matter of the USPSTF and ACOG endorsing [the ACS guidelines]." The USPSTF is currently updating its cervical screening guidelines, which could potentially help reconcile this discord between the guidelines and close the gaps in practice patterns.

ANAPHYLAXIS CLINICAL PRACTICE GUIDELINES

Late in 2023, the *Annals of Allergy, Asthma & Immunology* published updates to clinical practice guidelines related to anaphylaxis.[3] Recommendations include:

1. **Diagnosis:** Clinicians should obtain a baseline serum tryptase level in patients presenting with a history of recurrent, idiopathic, or severe anaphylaxis, particularly those presenting with hypotension.
2. **Anaphylaxis in infants and toddlers:** Because there are no criteria specific to this age group, clinicians should use current National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network or World Allergy Organization anaphylaxis criteria to assist in the diagnosis of anaphylaxis in infants/toddlers. Clinicians should prescribe either the 0.1-mg or the 0.15-mg epinephrine autoinjector dose for infants/toddlers weighing less than 15 kg.
3. **Beta-blocker and angiotensin-converting enzyme inhibitors:** Venom immunotherapy may be prescribed for patients with a history of insect sting anaphylaxis who are treated with beta-blocker or angiotensin converting enzyme inhibitor medication.
4. **Epinephrine autoinjectors:** Clinicians should routinely prescribe epinephrine autoinjectors to patients at higher risk of anaphylaxis. Optimal prescribing and use of epinephrine autoinjectors requires specific counseling and training of patients and caregivers.
5. **Mast cell disorders and anaphylaxis:** Clinicians should: a) order a bone marrow biopsy with staining for tryptase, CD25 immunohistochemistry and flow cytometry, and the KIT D816V mutation when there is strong suspicion for systemic mastocytosis; b) *not* rely on serum tryptase levels alone for diagnostic assessment of the likelihood that a patient does or does not have a clonal mast cell disorder; and c) measure baseline serum tryptase in patients with severe insect sting anaphylaxis, in all cases of recurrent unexplained anaphylaxis, and in patients with suspected mastocytosis.

FOCUSED UPDATE ON ADULT ACLS[4]

The American Heart Association (AHA) published a focused update in late December 2003 to address recent literature updates on several core topics that pertain to advanced cardiac life support (ACLS). The following are some key points.

1. **Vasopressor medications:** The AHA continues to endorse epinephrine as the first-line vasopressor choice in the setting of cardiac arrest. For nonshockable rhythms, clinicians are encouraged to administer epinephrine as soon as feasible (Class 2a). For shockable rhythms, clinicians should administer epinephrine after initial defibrillator attempts have failed.
2. **Nonvasopressor medications:** No nonvasopressor medications have been definitively proven to improve survival after cardiac arrest. Amiodarone or lidocaine may be considered for ventricular fibrillation or pulseless ventricular tachycardia if defibrillation attempts fail (Class 2b). The AHA also advises that the routine use of calcium, sodium bicarbonate, or magnesium in cardiac arrest is not recommended.
3. **Extracorporeal cardiopulmonary resuscitation (ECPR):** Based on updated publications since 2020 on extracorporeal cardiopulmonary resuscitation, the AHA offers a new Class 2a recommendation stating that the use of extracorporeal cardiopulmonary resuscitation may be beneficial for selected patients with cardiac arrest that is refractory to standard ACLS. Who those "selected patients" are, however, remains unclear.
4. **Percutaneous coronary intervention (PCI) after cardiac arrests:** Although post-arrest coronary angiography with possible PCI has been a source of debate in recent years, several recent randomized studies help to clarify which patients benefit from emergency angiography versus a delayed approach. The AHA gives a Class 1 indication for emergency angiography and a possible PCI for post-arrest patients with suspected cardiac cause and persistent ST-segment elevation after return of spontaneous circulation (ROSC).

   For patients without ST-segment elevation, the AHA gives a Class 2a recommendation for emergency angiography if the patient has an "elevated risk of significant coronary artery disease where revascularization may provide benefit, such as those with shock, electrical instability, signs of significant myocardial damage, or ongoing ischemia." In the absence of these factors, recent evidence strongly suggests that emergency coronary angiography can be performed in a delayed or selective strategy. The AHA also specifies that these recommendations exist regardless of the patient's post-ROSC neurologic status (Class 2a).
5. **Temperature control:** Nothing has changed here except the term "targeted temperature management" has been replaced with "temperature

Choosing Wisely

Originally published in the Fall 2012 issue of JLGH *in conjunction with the American Board of Internal Medicine's now-complete Choosing Wisely campaign, this edited reprint is offered to remind physicians of the importance of talking with patients about what tests, treatments, and procedures are needed — and which ones are not.*

RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF PHYSICIANS

❶ **In the evaluation of patients with simple syncope and a normal neurological examination, don't obtain brain imaging studies (CT or MRI).** In patients with witnessed syncope but no suggestion of seizure and no report of other neurologic symptoms or signs, the likelihood of a central nervous system problem being the cause of the event is extremely low and patient outcomes are not improved by brain imaging studies.

❷ **In patients with suspected venous thromboembolism (VTE) and a low pre-test probability of VTE, the initial diagnostic test should be a high-sensitivity D-dimer measurement, not imaging studies.** In such patients, i.e., those with a low pretest probability of VTE as defined by the Wells prediction rules, a negative high-sensitivity D-dimer measurement effectively excludes VTE and the need for further imaging studies. The American College of Radiology also includes pulmonary embolism in this context. They state that we should not be imaging for suspected pulmonary embolism (PE) without moderate or high pre-test probability. While DVT and PE are relatively common clinically, they are rare in the absence of elevated blood D-dimer levels and certain specific risk factors. Imaging, particularly CT pulmonary angiography, is a rapid, accurate, and widely available test, but has limited value in patients who are very unlikely to have a PE based on serum and clinical criteria. Imaging is not helpful to confirm or exclude PE for patients with low pre-test probability of PE.[5]

control." The AHA provides a Class 1 recommendation that post-arrest adults who do not follow commands after ROSC should receive treatment that is intended to maintain their core body temperature between 32°C and 37.5°C. That should be maintained for at least 24 hours.

NEW BREAST CANCER SCREENING RECOMMENDATION[6]

As with cervical cancer, breast cancer remains an area where conflicting recommendations between specialty groups persist. The incidence of breast cancer in women ages 40-49 rose 2% per year from 2015 to 2019.

Noting that foundational data on the effectiveness of breast cancer screening has not changed, the U.S. Preventive Services Task Force (USPSTF) earlier this year relied preliminarily on statistical modeling using data from six different breast cancer registries to analyze questions of starting and stopping ages and screening intervals.

The USPSTF recommendation grading scheme reports on both certainty of evidence and net benefits (benefits minus harms). A "B" recommendation is for moderate evidence of a moderate net benefit, and a "C" recommendation is for moderate evidence of a small net benefit. Recommendations are:

1. Screening is recommended every two years in women ages 40-74 years (B recommendation). The clinical considerations section states that conventional mammography or digital breast tomosynthesis (DBT, 3-D mammography) are both effective.
2. There is insufficient evidence for:
   - Screening in ages 75 and above.
   - Breast ultrasound or MRI for dense breast tissue.

Heterogeneous recommendations for breast cancer screening from other specialty societies complicate the public health message, although the USPSTF's new recommendation helps to reduce the differences. For instance, the American College of Obstetricians and Gynecologists suggests offering screening between ages 40-49 years and recommends screening every one to two years between ages 50 and "at least" 75 years.

The American Cancer Society suggests offering the option to start yearly screening between ages 40-44 years, recommends yearly screening routinely between ages 45-55 years, and recommends screening every one to two years for ages >55 years until life expectancy is limited to under 10 years.

Finally, the American College of Radiology recommends yearly screening starting at age 40 for average-age risk women but endorses assessing breast cancer risk beginning as early as age 25 for high-risk populations (lifetime risk >20%) and implementing both MRI surveillance and yearly mammograms.

As noted above, the USPSTF has now included 3-D mammography as an adjunct to conventional mammography and its recommended screening methods, noting that while there is a slight increase in positive predictive value with digital breast tomosynthesis, no trials have shown that difference in outcomes with its use.

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In addition to his duties as a contributor and board member of JLGH, Dr. Peterson serves on the board of the Lancaster Medical Heritage Museum and is director of its Publications Section, which can be found on the museum's website. To access the section, visit lancastermedicalheritagemuseum.org, and click on "PUBLICATIONS" near the top of the page to find a table of contents of the hundreds of Lancaster medical history articles available.

The museum is open Wednesday through Saturday, 11:00 a.m. to 3:00 p.m., except for the first Saturday of each month, when it is closed. Admission is free to Lancaster General Health employees with a badge and children under 3; $8:00 for all others.

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Cover photo by Michael K. Robinson II, MD, managing physician at Penn Medicine Lancaster General Health Physicians Family Medicine Red Rose.

Dr. Robinson's original photo above captures "Silent Symphony" at sunset. Designed by Lyman Whitaker, sculptor and public art manager for the City of Lancaster, the cluster of 42 wind sculptures at the northern edge of the city has welcomed locals and tourists to the Red Rose City for nearly a decade.

INTERESTED IN WRITING FOR *JLGH*?

The following is a summary of the general guidelines for submitting an article to *The Journal of Lancaster General Hospital*. Details are located online at JLGH.org.

- Scientific manuscripts are typically between 2,500-4,500 words. Perspective articles are usually shorter, and photo quizzes average about 725 words plus illustrations.
- Medical articles should report research, introduce new diagnostic or therapeutic modalities, describe innovations in health care delivery, or review complex or controversial clinical issues in patient care.
- Reports of research involving human subjects must include a statement that the subjects gave informed consent to participate in the study and that the study has been approved by the Institutional Review Board (IRB).
- Patient confidentiality must be protected according to the U.S. Health Insurance Portability and Accountability Act (HIPAA).
- The Journal of Lancaster General Hospital *does not allow chatbot tools such as ChatGPT to be listed as authors.* JLGH *editors warn authors that the use of these tools poses a risk for plagiarism with inappropriate use of citations, and we require that use of such tools be disclosed.*

Please contact the managing editor, Maria M. Boyer (717-544-8004), Maria.Boyer@pennmedicine.upenn.edu, to discuss submitting an article or for further information.

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EARN CME CREDIT

American Medical Association Category 2 activities consist of self-directed learning or courses that have not been through a formal approval process. According to the Pennsylvania State Board of Medicine, this includes "learning experiences that have improved the care [physicians] provide their patients." Reading authoritative medical literature – like medical journals – is one such activity.

For Pennsylvania physicians, more information and the Pennsylvania Board of Medicine CME Reporting Form are available at LGHealth.org/CME. *For advanced practice providers,* more information is available from credentialing organizations.

Physicians can also log credit and advanced practice providers can access transcripts through their eeds accounts online.

← Scan to access your eeds account.

← Scan for additional information and links to individual reporting instructions and forms.

Second Annual Pediatric Conference
"What's Bugging You?"
Update on Pediatric Infectious Disease
Thursday, November 7, 2024, 12:30-5:00 p.m., in-person only
Stager Conference Center, Lancaster General Hospital
Sponsored by the Penn Medicine Lancaster General Health Foundation

Topics and speakers include:

- Pearls and Perils: Diagnosis and Management in Infectious Disease — Sarah Long, MD
- How the Increased Use of Biologic Medications Is Affecting Pediatric Infectious Disease — Karen Ravin, MD
- Newborn Infections — Jessica E. Ericson, MD
- Vaccine Hesitancy and Vaccine Update — Lori Handy, MD
- Update on Antibiotic Resistance in Lancaster County and Upcoming Winter Viral Landscape — Nitin Patel, MD
- *Moderator — Pia Fenimore, MD*

Scan the QR code at right to register.

Other Upcoming CME Offerings at LG Health

Pediatric Grand Rounds
October 8, November 12, December 10, 7:00-8:00 a.m.

Department of Medicine Grand Rounds
October 2, November 6, 12:00 noon-1:00 p.m.

For the most up-to-date offerings and information from the LG Health Continuing Education Department, visit LGHealth.org/CME.