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For many business leaders, sales and marketing are interchangeable specialties with a singular goal: increasing revenue. However, sales and marketing teams should align together for a single objective. The truth is that they are distinct fields with differing strategies. Marketers often prioritize brand equity and capturing customers' attention, while salespeople focus exclusively on immediate customer conversions. And more importantly, sales needs marketing to succeed. This is especially true within the pharmaceutical industry. Digital marketing's rise makes it crucial for business leaders to grasp how marketing functions in the current landscape. And the best place to start is by answering a critical question: what is pharmaceutical marketing? Overview of Pharmaceutical Marketing Pharmaceutical marketing, often referred to as pharma marketing. Pharmaceutical marketing is a set of activities to increase awareness of and loyalty to pharmaceutical brands and products. Although its primary objective is to increase product awareness. Along with driving demand, and ultimately influencing healthcare professionals and consumers to choose a particular brand over others. Pharmaceutical marketing also aims to create a positive image of the drugs and the companies that manufacture them. It attempts to accomplish this by presenting scientific data, case studies, testimonials and other content persuasively. To do this, pharma marketers activate various channels, including digital marketing, traditional marketing (TV and Print), branding, direct-to-consumer advertising, and events. Explore More Relevant Articles on P360 Target Audiences in Pharmaceutical Marketing However, to be successful at increasing product awareness and driving demand. Pharma marketers must first understand who their target audience is and how to reach them. So, who is the target audience for pharma marketing? Healthcare Professionals: The primary target audience for pharma marketing is healthcare professionals (HCPs), including physicians, pharmacists, nurses, and other medical professionals. Pharmaceutical marketing aims to educate HCPs about the benefits and risks of various drugs. Their usage, administration, and to improve their prescribing behavior. Pharma companies can improve the chances of prescribing and selling their drugs by engaging with HCPs. Patients: Additionally, pharma marketing targets patients and caregivers to promote products and create brand awareness. Direct-to-consumer marketing has become increasingly prevalent. The Role of Digital and Mobile Marketing in Pharma While the target audience for pharma marketing is specific, pharma marketing strategies can vary. But they all have an underlying goal; to persuade the target audience to take action. The following are a few common channels pharma companies use to reach them. Pharma Digital Marketing: With most people's lives centered around the digital space. Online marketing tactics have become increasingly popular among pharma companies. They use interactive websites, social media, SEO, and targeted Ads to reach HCPs and patients. HCPs receive product info and data through newsletters, emails, digital catalogs, and text messages. For patient-centered marketing, the goal is to make people aware of a brand and educate them about a health issue. Digital marketing also offers valuable data to pharma companies. Which can help them understand the customer's needs better, make informed decisions, and create personalized marketing campaigns. Pharma Mobile Marketing: Mobile technology has simplified its engagement by offering a direct channel of communication. Platforms like the ZING Engagement Suite offer features like video conferencing, SMS messaging, and AI-powered automation. This allow HCPs and patients to communicate with pharma reps at any time, on any device. Mobile technology also accelerates the time it takes to receive information. Rather than scheduling an in-person meeting, HCPs and patients can connect with reps at their convenience. The Use of Direct-to-Consumer Advertising in Pharmaceutical marketing DTCA is a type of advertising that focuses directly on patients. DTCA promotes prescription drugs, medical devices, and health services. Supporters of DTCA say it can make people more aware of health issues and treatments, leading them to seek medical advice. Despite its criticisms, DTCA remains a popular marketing channel. Pharma companies that use it must be careful about creating accurate and informative advertisements. Engaging Healthcare Professionals: Conferences and Events Pharma companies often sponsor and participate in medical conferences and events. These conferences and events provide education and networking opportunities for healthcare professionals to exchange new product information and data. These conferences provide a platform to launch new products, engage with HCPs, and create a positive brand image. The conferences provide opportunities to showcase equipment, technologies, and services, and they offer an environment for networking and developing relationships with HCPs. For pharma companies, this is an opportunity. In these events they showcase their products and offer solutions to the challenges faced by HCPs. Networking and Information Exchange in Pharma Industry Pharma companies often hold educational events for healthcare professionals to learn about their products and how to use them. These events allow HCPs to learn more about the product, its features and benefits, and how it can solve a specific health problem. Events also allow pharma companies to demonstrate how their product can offer solutions to everyday healthcare issues. Webinars are also a cost-effective way of reaching HCPs and increasing brand awareness. The Role of Pharmaceutical Sales Representatives in Pharma Marketing Pharmaceutical sales representatives have been a crucial component of pharma marketing for decades. These representatives engage with HCPs directly to provide product information and samples. Training programs equip sales reps with the ability to understand the unique challenges and ideas in the healthcare industry. They are knowledgeable about the latest products and trends in the market. They offer a personal touch, which digital marketing fails to provide. They can also offer responsive and timely solutions to individual HCPs' needs. Navigating Regulatory Compliance in Pharmaceutical Marketing Pharmaceutical marketing poses several unique challenges that other industries do not face. Pharma marketers must balance the need for effective marketing with regulatory compliance, changing healthcare landscapes, public perception and trust, and ethical considerations. Here is a more detailed examination of each aspect. Regulatory Compliance: Pharmaceutical companies must adhere to strict regulations designed to protect public health. Balancing the need for effective marketing with regulatory compliance requires a nuanced approach. Pharma marketers need accurate messaging and regulatory approval before launching campaigns to avoid misleading information. To adhere to regulations, pharma marketers must walk a fine line between promoting and providing truthful information. Adapting to the Changing Healthcare Landscape The healthcare landscape is continually evolving, with advancements in medical technology and changes in treatment paradigms. Keeping marketing strategies aligned with emerging trends is crucial, and pharma marketers must stay updated with the latest developments. Doing so can ensure their marketing campaigns remain relevant and effective in a rapidly changing market. Building Trust: Ethical Considerations in Pharmaceutical Marketing Keeping the public's trust is always hard for people who market medicines. This is especially true when there are problems with how much drugs cost, worries about safety, and questions about what is right and wrong. Building and sustaining trust requires transparency and ethical marketing practices. Ethical pharmaceutical marketing involves providing true and accurate information to patients and healthcare professionals. Pharma marketers can also benefit from being transparent. They must communicate with stakeholders and respond to inquiries or concerns to rebuild trust. Balancing Transparency and Promotion Striking a balance between providing necessary information about pharmaceutical products and avoiding overly promotional tactics is another critical consideration. Patients and healthcare professionals should receive accurate, unbiased information to make informed decisions. That's why transparent communication about the benefits and risks of pharmaceutical products is essential. Concealing or downplaying potential side effects can erode trust and lead to ethical concerns. Avoiding Unfair Competition Unfair competition practices, such as spreading misinformation about competitors' products, undermine the industry's integrity. Pharma marketers should always focus on the merits of one's own products rather than disparaging others. The Crucial Role of Pharmaceutical Marketing in Advancing Healthcare There is no doubt that pharmaceutical marketing plays a pivotal role in promoting innovative medical solutions. The term "pharma marketing" often elicits varied responses, ranging from skepticism to admiration. Its significance lies in its ability to educate, inform, and connect stakeholders in the healthcare ecosystem. It is a dynamic and indispensable aspect of the healthcare industry, and it helps pharma companies succeed by achieving the following. Pharma marketing is a conduit for disseminating critical information about pharmaceutical products, medical devices, and healthcare services. The healthcare world is always changing fast with new science. This makes it hard for doctors, nurses, and patients to keep up with new things. Marketing helps by making sure everyone knows the latest information about new treatments, medicines, and medical tools. Pharmaceutical Marketing: Bridging Information Gaps Pharma marketing helps healthcare professionals learn how drugs work, their good effects, and their safety. Knowing this is important for selecting the correct treatments for patients, especially in areas with numerous new options. Accelerating Patient Access to New Treatments One of the primary goals of pharma marketing is to facilitate timely and widespread access to innovative healthcare solutions. Through targeted promotional campaigns, pharmaceutical companies can raise awareness about breakthrough treatments and medications. This ensures that healthcare professionals receive information about new options for managing diseases and improving patient outcomes. For patients, pharma marketing can be empowering. Awareness campaigns educate individuals about specific medical conditions and inform them about available treatment options. This knowledge enables patients to engage in more meaningful conversations with their healthcare providers. As they actively participate in treatment decisions, and, in some cases, advocate for their own health. 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By creating demand for innovative products, marketing efforts contribute to the financial resources needed for ongoing research and development. The revenue generated from successful marketing campaigns allows pharmaceutical companies to reinvest in creating new drugs, medical devices and therapies. The pharmaceutical market is very competitive. This makes companies work hard to create new and better products. They need to use good marketing to tell people about these new products. If they don't, they won't make enough money to pay for the research and tests needed to make new treatments Educational Role of Pharma Marketing for Healthcare Professionals Healthcare professionals like doctors, and others need clear and complete information to choose the best care for their patients. Pharma marketing serves as an educational resource, providing healthcare professionals with insights into the latest clinical data, treatment guidelines, and emerging therapeutic approaches. Through avenues such as medical conferences, seminars and digital platforms, pharmaceutical companies engage healthcare professionals in discussions about disease management and treatment options. This continuous exchange of information enhances the expertise of healthcare providers, contributing to improved patient care and outcomes. Addressing Public Health Challenges Through Pharma Marketing Pharma marketing is important for public health. It helps people learn about how to prevent diseases, manage them, and know about treatments. Pharma companies start campaigns to teach people about health issues. This helps people act to lower the chances of getting sick. For instance, they do campaigns on vaccines, handling diabetes, or mental health support. These campaigns add to public health work. Pharma companies use their large marketing networks to spread health information far and wide. This helps many different people learn more about how to prevent health problems. Supporting Patient Assistance Programs Pharmaceutical companies often collaborate with advocacy groups and establish patient assistance programs to ensure that individuals with financial constraints can access essential medications. These programs, supported and promoted through marketing efforts, provide discounted or free medications to eligible patients, addressing socioeconomic disparities in healthcare access. Pharma marketing supports programs that help people get healthcare. This means that those who need it can receive important treatments. Pharmaceutical Marketing in the Era of Personalized Medicine The healthcare landscape is continuously evolving, marked by technological advancements, changing treatment paradigms, and a greater emphasis on personalized medicine. Pharma marketing plays a crucial role in helping stakeholders navigate these dynamics by providing information about emerging therapies, diagnostic tools, and treatment modalities. Through targeted educational campaigns, pharmaceutical companies prepare healthcare professionals and patients for the integration of novel technologies and treatment approaches into routine clinical practice. Being flexible is key in healthcare. It helps meet the changing needs of patients and the community. Conclusion:- The Future of Pharma Marketing Even though pharma marketing is complex and always changing. Pharmaceutical marketing is a very important part of making progress in healthcare. From bridging information gaps and accelerating patient care to fostering research and development, the impact of pharma marketing reverberates across the entire healthcare ecosystem. By serving as a conduit for knowledge, promoting preventive measures and supporting patient assistance programs. It contributes not only to the success of individual pharmaceutical products but also to the overarching goal of advancing public health. And as the healthcare industry continues to evolve, so will pharma marketing. Stay tuned as we continue to write about this multifaceted discipline that is critical to patient health. Share — copy and redistribute the material in any medium or format for any purpose, even commercially. Adapt — remix, transform, and build upon the material for any purpose, even commercially. The licensor cannot revoke these freedoms as long as you follow the license terms. Attribution — You must give appropriate credit , provide a link to the license, and indicate if changes were made . You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use. ShareAlike — If you remix, transform, or build upon the material, you must distribute your contributions under the same license as the original. No additional restrictions — You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits. You do not have to comply with the license for elements of the material in the public domain or where your use is permitted by an applicable exception or limitation . No warranties are given. The license may not give you all of the permissions necessary for your intended use. For example, other rights such as publicity, privacy, or moral rights may limit how you use the material. We often encounter confusion between the terms strategy and tactics. Sometimes, when strategy is discussed, blogging is mentioned but to me, blogging isn't necessarily a high-level strategy, rather more a strategic tactic or put simply, a tactic to undertake the strategy or the strategic direction of the proposed marketing campaign. Another way to put it: The strategy is the overall campaign plan and the tactics are the actual means to achieve the objective of the strategic plan. The strategy is the planning, where the latter is the doing. So for this post we will look at strategy (this e-book explores 25 pharmaceutical marketing tactics and techniques). Subscribe for marketing insights via email So when we look to define a pharmaceutical marketing strategy or a range of strategic marketing options, we need to ask ourselves the following questions in accordance to our marketing/organisational objectives:How will our marketing activities help make sales?What market trends are emerging that we need to respond to?What position will we strive to achieve?Which pharma market segments will be targeted with which propositions?What communication strategies will be used to support customer acquisition?What experience will we look to create for our audiences?How can we differ from our competitors?At this stage, we're not so much looking to reach an audience per se, we're actually looking at how and what we will be saying to that audience once we reach them. In the most basic language, a pharmaceutical marketing strategy looks at the objective of a marketing team or organisation and defines how to get there.In this post of pharmaceutical marketing strategies, we will look at some avenues to "get there" and achieve objectives as well as provide some examples of marketing strategies which you will have seen before.Strategic pharmaceutical marketingPharmaceutical organisations regardless of where it sits within the supply chain or whether it focuses on a B2B or B2C audience will need to adopt a particular marketing strategy to effectively sell its products and services. We'll run through some of the most common pharmaceutical marketing strategies next. 1. Market/product development strategyA product/market development strategy concerns developing new products or modifying existing products and offering those products to current or new markets. These strategies typically surface when there is little opportunity for growth in an organisation's existing market.The four most common strategies in this category derive from the Ansoff Matrix (below): market penetration (growing sales of an existing product in existing markets), market development (launching an existing product in a new market), product development (introducing an existing product into a new market) and diversification (introducing a new product into a new market).Your pharmaceutical product or service will be promoted in accordance with the Ansoff Matrix almost every time and can dictate the marketing strategy you will adopt. For example, we see so many partnerships and mergers in this industry, where pharmaceutical organisations combine their resources and leverage their strengths to increase market share in this manner. Should a pharmaceutical organisation want to sell more products in current markets, it might decide to invest more in its marketing budget. A search marketing (SEO) strategy looks to increase visibility on search engines to increase the number of visitors arriving at a website and its web pages. A strategic approach that takes time, but the results that manifest over this time are often long-term and can achieve an objective of becoming more visible, certainly in current markets. More and more pharmaceutical organisations are adopting more digital-first strategies such as this to increase visibility. For more, please see this article on Pharma SEO.DIRECT SALESThe traditional method of employing sales personnel and then deploying those in the regions and markets where you are looking to generate new customers is still widely used today. This is certainly the case in the B2B pharmaceutical markets where face-to-face contact is still a large enabler of business. This non-marketing strategy needs guidelines on how to recruit salespeople who understand how to sell products in new and often emerging markets but has proven (and still does) to be effective. 2. REVENUE STRATEGYA revenue model strategy (or more casually, a business strategy) is a strategy usually focused on forming a product or service whereby advertising or licencing revenue can be generated subsequently, or more broadly, a strategy focused on generating revenue. Magazines and publications follow this strategy, albeit on different levels where a customer-base is usually built to be leveraged. In this case, the editorial team is commissioned to write content that is packaged into a printed publication, as well as for an online audience that can subscribe, that is then used to drive advertising revenue from organisations that wish to advertise to this audience. Co-branded promotions and list rentals are hugely popular in this respect and are not limited to media and publishing organisations alone, as many organisations outside of this space can adopt this strategy to reach its business goals. Pharmaceutical organisations also outsource at least part of their R&D processes to other pharmaceutical organisations and according to AMR Research, today most pharmaceutical and biotech companies outsource at least a proportion of their clinical trial management process, another example of how pharmaceutical are perusing cost/revenue-based strategies.AFFILIATE MARKETINGAffiliate marketing - a type of performance-based marketing in which a business rewards one or more affiliates for each visitor or customer brought by the affiliate's own marketing efforts - broadly falls within this category. This is the case as an affiliate program's sole purpose is to sell products with minimal marketing spend waste as affiliates are paid on a per-sale basis.EMAIL MARKETING AND LIST BUILDINGOrganisations that rent assets and inventories fall within this category, and email marketing has become a popular channel in this respect. Organisations can rent email lists (for a price) so that other organisations can sell their products to the subscribers within that email list. This is an interesting concept as, for the most part, the owner of the email list will not sell its own services to its own list. For more, see this article on B2B email marketing best practices.3. TARGET MARKETING STRATEGYEvery pharmaceutical marketing strategy will involve an element of targeting. Targeting enables organisations to narrow their focus and aim marketing campaigns and messages at a specific segment of the market, thus becoming more relevant to the audience and increasing the chances of conversion into a customer or client. Essentially focusing on customers that an organisation can serve best.A targeting strategy often involves focusing on organisations via one or more of the following attributes: Most profitable customers, larger or smaller organisations, loyal customers, customers that are not brand-loyal and employees of a particular organisation (see post on ABM strategies and tactics) for B2B organisations. Depending on the pharmaceutical organisation type, this process is potentially a two-step process. The first targeting exercise is the customer from a B2B perspective and then the end-user from a B2C perspective. A holistic view on the segmentation process, for example, could enable an OTC and Nutraceutical marketing organisation to develop insights and perspectives that are essential for developing a winning strategy in the OTC and Nutraceutical market. Markets consist of various demographic characteristics, needs and behaviours, therefore products/services and marketing messages may not relate to all of these people. So, strategic segmentation provides an opportunity to target specific messages and campaigns towards specific audiences. Creating buyer personas is a great way to start the process, as you will immediately understand the audience(s) which you are targeting to tailor your content towards. Lifecycle targeting is also another option to consider, which can be done by targeting content at your audiences during specific stages of the buyer's journey.PRODUCT AND SERVICE POSITIONINGAlthough it's sometimes normal that a competitor's product and service offering differs online versus offline, it is often that an organisation's overall offering is very similar to that of a competitor's. With this in mind, positioning your products/services, organisation and brand - and giving it its own USP - can be the differentiation that tips offering as the most desired solution from the competition.4. POSITIONING AND DIFFERENTIATION STRATEGYThe section above briefly touches on positioning and differentiation in the context of segments and sub-markets - elements concerned with the customer. This strategy, on the other hand, assumes that the organisation's marketing strategy indeed takes into account the customer's perception of the offering but relative to those of the competition. Organisations can position their products and services according to four variables: Product quality, service quality, price and fulfilment time. Reviewing your internal strengths and comparing them to those of your competitors, a differentiation strategy that positions your offering above those of your competitors can be achieved giving the organisation a competitive advantage.To bring the strategy to life, the pharmaceutical organisation can define the product strategy, as PharmExec state: "A product positioning statement is a series of phrases or sentences that articulate the drug's unique selling proposition, typically including the brand name, product category, target customers, key benefit, and primary competitive differentiation." Branding is how organisations are perceived in the minds of the audience. Organisations can differentiate themselves from the competition with a brand strategy. More than simply a name, term, design, or symbol, a brand is the recognisable feeling a product or business evokes. Brand management begins with an analysis of how a brand is currently perceived in the market and then proceeds to plan how the brand should be perceived if it is to achieve its objectives.ONLINE/OFFLINE VALUE PROPOSITIONA value proposition is not just a statement of the benefits of the products and services to reinforce the core proposition to differentiate it from the competitors. It also acts as a driver for developing content and communicating messages that will strategically fit with its indented audience, providing a direction for all marketing messages.5. CUSTOMER ENGAGEMENT STRATEGYA popular strategy, that one way or another, most companies will adopt. The strategy aims to create compelling content and experiences and encourages interaction and participation. With the development of technologies and the growth of marketing platforms and channels, a customer engagement strategy is highly common for most B2C organisations, as well as B2B brands who are looking for a two-way dialogue with their audiences. This is certainly the case for us here at Orientation Marketing. The aim here is to develop a community around the brand whereby audiences can interact with certain content.In the pharmaceutical industry, more so big pharma, and just like most other consumer-facing industries, there are more products and more messages subsequently meaning more noise. PharmaPhorum explores this and looks at key trends affecting a customer engagement strategy in the pharmaceutical industry such as the changing audience, rise of medical affairs and the development of new patient support programmes. Content marketing is the process of writing and publishing content to educate potential customers about products and services or solutions to common problems for target audiences. Content marketing is an effective strategy to engage with audiences just as it is within a market/product development strategy, for example. To enter new markets, content marketing (or inbound marketing) can help with the positioning of a new product, generate awareness and generate new leads.SOCIAL MEDIA STRATEGYSocial media platforms provide an audience of highly engaged people, who can be targeted both organically and via paid means to help achieve marketing objectives. The scope of social media optimisation also includes the incorporation of features such as sharing and commenting on social media platforms and on company websites. Such a strategy can incorporate all of or a range of networks, such as Twitter, LinkedIn, Facebook and Instagram, to only adopting just one which is most frequently used by your particular audience. Paid social media marketing allows you to build a strong online presence of your brand on social media platforms quickly, with the caveat that investment is required, usually in the form of pay-per-click. A multi-channel marketing communications strategy reviews the different types of customer contact with an organisation to then determine how these touchpoints can be incorporated within a marketing plan to reach objectives. This strategy involves both online and offline channels and can connect outbound call with a website and email, for example.Multi-channels strategies derive from an internal audit to determine customer channel preferences as well as the preferences of the organisation usually based on internal processes. Pharmaceutical organisations are required to consider many elements of the strategy, such as customer insight, the experience as well as its internal capability when adopting multi-channel strategies.Two common marketing strategies that pharmaceutical organisations can broadly adopt arise from this sort of strategy. A customer acquisition strategy defines the best mix of media and engagement tools (lead generation and product offers) to gain new customers by targeting them and reaching them through online and offline customer journeys. This strategy involves a marketing focus of generating new business leads and customers, often in the form of inbound sales-related enquiries. An essential component for most organisations.CUSTOMER RETENTION STRATEGYA customer retention strategy focuses less on generating new customers and focuses more on keeping current customers - customers who you've already invested in and earned - happy, loyal and buying from you. This might include delivering service that's consistent with your value proposition and brand or cross-selling, up-selling, asking for referrals from existing customers and developing programmes that increase customer loyalty. Customer services teams are in place for this very reason.STRATEGY AS A PATH TO REACH YOUR OBJECTIVESStrategy, as a word, is derived from the Greek "strategos" originally intended to mean "the art of the general." Those generals would never have engaged in hand-to-hand combat meaning that your pharmaceutical marketing strategy, similarly, defines how you will deploy your armies and resources and the six strategies listed in this post are prime examples of this at work in the pharmaceutical and related industries.Marketing to patients and doctors require distinct strategies, just as it would between organisations within the B2B supply chain, but pharmaceutical marketing, in general, involves the same principles that you find in any other industry. Chris Lawson Healthcare Marketing Blogs – MediVerticals This article provides an overview of the education, experience, skills, and networking required to pursue a career in pharmaceutical marketing. It covers 9 proven strategies, including the 4Ps of marketing, and offers insights into HCP digital behaviors and personalization in modern healthcare. A pharmaceutical sales representative markets and sells pharmaceutical medications and devices to medical providers, educating them on medications and selling them.To advance their careers in the pharmaceutical industry, professionals should gain relevant experience, network, build a strong online presence, and obtain certifications or advanced education. To become a pharmaceutical sales representative, one should earn a high school diploma or GED, obtain a bachelor's degree, and consider earning a degree in a relevant field.A job in pharmaceutical marketing involves product and service development, research, communication projects, PR, sales programs, customer relations, and events. Many pharmaceutical companies offer internships in their market access departments, providing practical experience. To get into pharmaceutical sales, meet job requirements, hone the right skills, network, apply, and apply for positions.Tips for getting into pharmaceutical sales include attending networking events, reaching out to healthcare providers, and scheduling informational interviews. By following these strategies, individuals can gain practical experience and develop a strong foundation in the field of pharmaceutical marketing. Pharmaceutical Marketing & Commercialization | CAREER ADVICE FOR PharmD, MPH, MS, MSN, BSc StudentsPharmaceutical Marketing & Commercialization | CAREER ADVICE FOR PHARMD, MPH, MS, MSN, BSc Students Get private …How to get into market access pharma?Successful applicants for the Market Access Specialist position must hold a master's degree in life sciences, medical, or economics, have previous pharmaceutical experience, and have a proven track record in pharmaceutical market access. The company is known as MSD worldwide, except in the United States and Canada, where it is known as Merck and Co Inc, Rahway, NJ USA. The website is intended for residents of the United States and Canada, and the company is known as Merck and Co., Inc., Rahway, NJ, USA.(Image Source: Pixabay.com)What does a pharma marketer do?Pharmaceutical marketing is a field that focuses on the communication, differentiation, and commercialization of pharmaceutical products, including specialist drugs, biotech drugs, and over-the-counter drugs. It is regulated by international and national agencies like the Food and Drug Administration and the European Medicines Agency, as well as local regulations from government or industry associations like Pharmaceutical Research and Manufacturers of America or the European Federation of Pharmaceutical Industries and Associations (EFPIA).Read also: How Can I Use My Mac To Create Flyers?Marketing to healthcare providers involves three main forms: activity by pharmaceutical sales representatives, provision of drug samples, and sponsoring continuing medical education (CME). Gifts embossed with pharmaceutical product names are prohibited by PHRMA ethics guidelines since 2008. A 2010 Physician Access survey found that half of the 237, 000 medical sites representing 680, 000 physicians prefer or require an appointment to see a representative, while 23 won't see representatives at all.The most accessible physicians for promotional purposes are allergists/immunologists, orthopedic specialists, and diabetes specialists. Diagnostic radiologists are the most rigid about allowing details, followed by pathologists and neuroradiologists.How to go into pharmaceutical marketing?To become a pharmaceutical sales representative, one must first obtain a high school diploma, GED, bachelor's degree, or a graduate degree. Additionally, one should consider pursuing relevant certification, developing a robust professional network, enhancing one's skill set, and preparing a comprehensive resume and cover letter.(Image Source: Pixabay.com)How to break into the pharmaceutical industry?The pharmaceutical industry offers numerous opportunities for graduates with a professional degree in pharmaceuticals, including discovery, production, formulation, administration, and manufacturing. To get a job in the industry, follow these six steps: obtaining the required qualifications, developing skills, gaining experience through internships, updating your resume, applying for jobs, and pursuing higher studies. Essential skills needed for success include communication, accuracy, interpersonal, organizational abilities, ethical attitude, curiosity, and technical aptitude.Various job options in the pharmaceutical sector include researchers, sales representatives, pharmacy technicians, drug regulatory authority officers, quality control executives, and pharmaceutical subject teachers. To ensure success, it is essential to understand the standard career path and the skills needed to be successful in the pharmaceutical industry.What is the best degree for pharmaceutical sales?In the contemporary job market, employers tend to favor candidates with a robust scientific background, particularly in fields such as pharmacology, chemistry, biology, medicine, mathematics, and statistics. Additionally, they often seek individuals with business training in sales and negotiation skills.(Image Source: Pixabay.com)What is the difference between pharmaceutical marketing and selling?Marketing involves generating leads or prospects, while sales involves converting these leads into purchases and orders. Marketing is a long-term process that builds a brand in the market, directly related to the customer's needs, while sales are short-term for finding customers and converting them into exchanges. The success of an organization is entirely dependent on sales and marketing. Pharmaceutical and biotech marketers use various strategies and planning to reach consumers and professionals, using various marketing channels, sales strategies, and promotional activities for revenue generation.Read also: How Much Does A Professional Seo Blogger Charge?They also use various questions for pharma interviews related to body systems, pharmacology, career options, starting a pharma marketing company, and the anatomy and physiology of the ear, nose, and throat.(Image Source: Pixabay.com)What is the best job in the pharma industry?The pharmaceutical industry is a rapidly evolving field with a wide range of roles, including pharmacists, clinical data managers, regulatory affairs specialists, biostatists, quality assurance/quality control professionals, pharmaceutical sales representatives, research and development scientists, and medical writers. These positions require a combination of skills and expertise to excel in the rapidly evolving healthcare sector.The most in-demand jobs in the pharmaceutical industry include clinical data managers, regulatory affairs specialists, biostatists, quality assurance/quality control professionals, pharmaceutical sales representatives, and R and D scientists. These positions require a combination of technical skills and expertise to succeed in the rapidly evolving pharmaceutical industry.Is market access a good career?Market Access careers offer challenging yet rewarding careers, with smaller Pharma teams offering fewer job opportunities. Most candidates opt for the consultant career path, which includes Analyst, Senior Analyst or Associate Consultant, Consultant, Senior Consultant, and Director positions. The industry's typical career progression options include Analyst, Senior Consultant, and Director.Why do you want to join pharma marketing?Pharma is a prestigious and prestigious industry known for its competitive compensation packages and excellent benefits. It is a field that impacts human health and offers job stability, growth opportunities, and a profound impact on human health. Working with a PCD pharma franchise company in Ahmedabad or other cities allows individuals to experience the best of the pharma industry. Tesni Pharma, one of the best PCD pharma franchise companies in India, offers an enriching environment for building a meaningful career in the pharmaceutical industry. The job offers opportunities for making big changes, learning, feeling vital, and receiving well-paying salaries.(Image Source: Pixabay.com)What are the richest jobs in the medical field?The medical field offers a diverse range of rewarding professions, including ophthalmologists, pharmacists, dentists, pediatricians, nurse anesthetists, podiatrists, obstetricians-gynecologists, and internal medicine physicians. These positions offer high salaries, duties, and the potential for financial security. To find a job in the medical field, it is essential to understand your choices and make an informed decision.The top 12 highest-paying jobs in the medical field include ophthalmologists, pharmacists, dentists, pediatricians, nurse anesthetists, podiatrists, obstetricians-gynecologists, and internal medicine physicians. These positions provide a high level of financial security and a competitive edge in the medical industry. Becoming a Certified Pharmaceutical Sales RepresentativeWatch Dr. William Soliman explain more about the Pharmaceutical Representative Certification (PRC). Launch Your Path to …(Image Source: Pixabay.com) A pharmaceutical marketing degree combines conventional business training with an education in pharmaceuticals and medical science. Scholars might take an array of courses that cover disciplines such as biology, chemistry and anatomy, as well as topics like health care law, supply chain management and marketing strategy. In 2016, the pharmaceutical industry spent $29.9 billion on medical marketing in the United States, including $20.3 billion for marketing directly to health care professionals. Of this spending, $5.6 billion was for prescriber detailing (mainly face-to-face visits), $13.5 billion for drug samples, and $979 million for direct physician payments.1 The United States has, by far, the highest prescription drug prices in the world.2 Market exclusivity is an important factor in high U.S. drug prices; on average, top-selling pharmaceuticals in the United States have a patent exclusivity of 14.5 years.2,3 Additionally, government-funded health plans are forbidden from negotiating lower prices for patients.2 These system processes maintain high drug prices that directly harm patients, especially those in marginalized communities.4–6 Knowing that the high price of drugs is a major detriment to public health in the United States and that the pharmaceutical industry spends vast sums marketing to health care professionals, physicians should refuse visits, gifts, payments, and drug samples from pharmaceutical representatives. Physicians Should Not Visit with Pharmaceutical Representatives Pharmaceutical representatives are trained to influence physicians, and they are effective.7,8 Visits from industry representatives often come with gifts and food, leading to low-value prescribing that is not evidence based.7,9 Pharmaceutical representatives seek to change the prescribing habits of a physician.8 Physicians claim that their behavior is not changed by industry interactions but admit to believing that other physicians can be influenced.10 Physicians who think they can accept gifts and spend time with industry representatives and not be influenced are in a position of cognitive dissonance.10 Time spent with these representatives is wasteful because ethical physicians are required to read about new drugs extensively to counteract false information provided by the representatives.11 In the words of family physician and ethicist Howard Brody, "Physicians ought to refuse to visit with representatives as a matter of both professional integrity and sensible time management."12 Physicians Should Not Accept Gifts, Food, or Direct Payments from Industry Gifts, even small ones such as pens and notepads, influence behavior.13,14 Direct payments from a pharmaceutical company increase the likelihood that physicians will prescribe that company's medications.13–15 This arrangement violates our ethical obligation to put the patient first. Unsurprisingly, patients report that they are not comfortable with this arrangement.16 Considering that many patients experience hardship because their medications are too expensive, perhaps industry could redistribute the $20.3 billion they spend on physician marketing toward lowering drug costs. Physicians Should Refuse "Free" Samples for Their Patients It is tempting to think sample medications help underserved patients, but samples do more harm than good. Medications in sample closets are not novel or useful and are often expired or inappropriately used by physicians and staff members.17–19 Sample medications in family medicine offices are brand-name medications delivered by industry to increase sales of the drug. A sample closet is actually a marketing closet.20 Samples are rarely first-line medications, recommended by guidelines, or superior to less expensive generic alternatives.17,21 Use of sample-closet medications leads to nonrational prescribing.22 Sample-closet medications are more likely to be used by patients who have health insurance and not by patients most in need.23 A patient started on an expensive brand-name drug is likely to continue that drug.8 Use of sample-closet medications increases the cost of medications for patients, both out-of-pocket and total cost.24 The $13.5 billion the pharmaceutical industry spends annually on sample medications is not designed to help patients; it is designed to increase sales of brand-name drugs. The Good News: Physician Interaction with Industry Is Decreasing Numerous national organizations and experts have called for limiting physician-industry interaction.25 The Physician Payments Sunshine Act, part of the 2010 Affordable Care Act, required the industry to report all gifts to physicians starting in 2014.26 There is evidence that this reporting, with strict legislative action, has decreased interactions between physicians and industry.27,28 All interaction (e.g., detailing, samples, gifts, direct payments) between physicians and industry has decreased slightly over the past decade, from 84% in 2009 to 72% in 2017, according to surveys of physicians.29,30 In 2017, 55% of physician offices reported accepting samples vs. 64% in 2009.29,30 Family medicine residency programs have even more substantially decreased their interactions with industry. In 2019, 64% of programs did not allow the use of samples, the acceptance of food or gifts, industry-sponsored residency activities, or other industry interactions, compared with 26% in 2008.31 As of 2019, 86% of family medicine residencies do not accept samples, and 84% do not allow visits with industry representatives, a substantial increase from 52% and 43%, respectively, in 2008.31 Program directors cite institutional policy and ethical concerns as the main factors driving a decrease in industry interaction.31 Restricting contacts with industry during physician training is especially important to promote evidence-based prescribing because practice habits form during this important time in a physician's career. The high cost of prescription drugs in the United States is a major public health challenge. This high cost is driven by prescribing of expensive brand-name medications, which is influenced heavily by the pharmaceutical industry spending billions of dollars to market directly to physicians. Physicians should refuse gifts, samples, direct payments, and other industry interaction to avoid perpetuating an unjust health system. It is the professional responsibility of a physician to promote social justice, commit to a just distribution of finite resources, prioritize patient welfare, and not compromise integrity with conflicts of interest.32 Editor's Note: American Family Physician has a strict policy when it comes to authorship and conflict of interest (. In addition to reviewing disclosure forms submitted by authors, we routinely search public databases of physician-industry interactions to make sure there are no conflicts that were inadvertently omitted. During this search, we frequently uncover numerous reports of lunches and dinners provided by pharmaceutical companies. We carefully review each one to see whether the reports are relevant to the topic of the article and to determine the degree of financial relationship (i.e., a lunch or two vs. hundreds of dollars for meals). Rarely has an author been disqualified based on these meals alone; however, disclosures have sometimes been published with the articles, and the option of disqualification is possible for significant meal payments to avoid the perception of bias.—Sumi Sexton, MD, Editor-in-Chief Dr. Brown is a contributing editor for AFP. Page 2 Am Fam Physician. 2021;104(4):351-352 Author disclosure: No relevant financial affiliations. In 2016, for the first time, less than one-half of practicing physicians had an ownership stake in their own practices.1 The most recent American Medical Association Physician Practice Benchmark Survey reveals that this trend continues.2 More physicians are identifying as employees instead of owners, with family physicians being the second most likely specialty to be employed. This trend has significant implications for reimbursement and practice patterns, and potential impacts on physician burnout if scope is limited by employers.2,3 The Robert Graham Center, in conjunction with researchers at the American Board of Family Medicine and IBM Watson Health, examined employment trends in the report "Primary Care in the United States, A Chartbook of Facts and Statistics." 4 Employment status of primary care physicians was analyzed using 2016 National Ambulatory Medical Care Survey data (Figure 1). Slightly less than one-half (49%) of primary care physicians owned their own practices. Most working physicians were employees of a non–physician-owned practice. The increasing percentage of employed physicians may be due to a variety of factors, including greater financial stability.5 Younger physicians are also reported to be less attracted to the entrepreneurial aspect of private practice ownership.6 Although these trends may reflect financial and lifestyle decisions, the implications of a largely employed primary care workforce are not necessarily positive. For example, employers in multispecialty practices could be defining or limiting the scope of practice of their physicians, which has implications for training, physician satisfaction, and health care costs.3,7 The impact of employment status on health care quality is still unclear. Some studies suggest that it has no relationship to health care quality.2 Other studies show that primary care ownership is associated with less use of quality improvement process measures in comparison with federally qualified health centers and hospital-owned practices.8,9 In addition, hospital-owned practices demonstrated greater use of evidence-based chronic care management processes, which may improve care coordination.9 Although there are benefits to choosing employment instead of ownership, the disadvantages for primary care physicians and their patients may be significant and are worth further exploration. The information and opinions contained in research from the Graham Center do not necessarily reflect the views or the policy of the AAFP. This series is coordinated by Kenny Lin, MD, MPH, deputy editor. A collection of Graham Center Policy One-Pagers published in AFP is available at . One-Pagers are also available at . Page 3 What is an effective approach to treatment-resistant depression in adults? Atypical antipsychotics can be an effective augmentation therapy for adults with treatment-resistant depression. According to a Cochrane review, adding quetiapine (Seroquel) to anti-depressant therapy reduces symptoms below the remission threshold (number needed to treat = 9), and the number of people who stop using the medicine increases only at the highest dosage. Augmentation with cariprazine (Vraylar) or ziprasidone (Geodon) improves the clinical response; however, the benefit is offset by increased treatment dropouts. How should patients with degenerative cervical myelopathy be evaluated and treated? Magnetic resonance imaging with and without contrast is the modality of choice for patients with suspected degenerative cervical myelopathy. Surgical management is indicated for patients with moderate to severe myelopathic signs and symptoms; however, even with surgery, many patients have residual deficits. What are examples of clinical scenarios where diagnostic imaging is not indicated? Do not perform imaging in patients with primary headache disorders without new or progressive features who have normal neurologic examination findings. Do not perform plain chest radiography for preoperative evaluations or baseline testing during hospitalizations for patients who are asymptomatic. Do not perform imaging in patients with acute (less than six weeks) low back pain and no red flag findings on history or physical examination. What is the first-line treatment approach for patients with an eating disorder? Family-based therapy should be a first-line approach for youths with anorexia nervosa and bulimia nervosa, and medications should not be used as monotherapy. If medications are used for adjunctive therapy, lisdexamfetamine (Vyvanse) can be effective in reducing binge-eating behaviors in persons with binge-eating disorder. [corrected] Are vitamin K antagonists effective in preventing recurrence for patients with distal (below knee) DVT? According to a Cochrane review, vitamin K antagonists reduce the recurrence of deep venous thrombosis (DVT) and venous thromboembolism (number needed to treat = 17), but not pulmonary embolism, compared with no anticoagulation or placebo. A treatment duration of three months or more reduces these recurrences, compared with six weeks of therapy. The risk of clinically relevant nonmajor bleeding (number needed to harm = 23), but not major bleeding, is increased with anticoagulation. Additional Online Only AFP Clinical Answers How does regular exercise impact the occurrence, severity, or duration of acute respiratory tract infections? Regular exercise may reduce the overall severity of acute respiratory tract infections and the number of days with symptoms in adults, according to a Cochrane review. There is no evidence that exercise reduces the overall occurrence or duration of these infections. How should hip pain in adults be evaluated? Standing anteroposterior hip and pelvic radiographs are the first choice if performing imaging for a patient with undifferentiated chronic hip pain. If the patient's history suggests a labral tear, stress fracture of the femoral neck, or early avascular necrosis, magnetic resonance imaging should be performed. Consider ultrasonography or magnetic resonance imaging to evaluate for gluteus medius tendon tears in patients with greater trochanteric pain syndrome not responding to conservative therapy. How should dysphagia be managed? Patients younger than 50 years who have esophageal dysphagia and no other worrisome symptoms should undergo a four-week trial of acid suppression therapy before endoscopy is performed. Patients with apparent oropharyngeal symptoms and a negative evaluation should be referred for esophagogastroduodenoscopy (EGD) to rule out esophageal pathology. EGD is recommended for the initial assessment of patients with esophageal dysphagia, and barium esophagography is recommended as an adjunct if EGD findings are negative. Editor's Note: Several of the answers above first appeared in the new AFP Clinical Answers email, which is sent each month to recipients of the AFP email table of contents. Sign up to receive AFP emails. Page 4 Does maintenance therapy with antipsychotic drugs prevent symptom relapse in patients with schizophrenia? Compared with placebo, using antipsychotic drugs for maintenance therapy in patients with schizophrenia is associated with relapse prevention at seven to 12 months (number needed to treat [NNT] = 3; 95% CI, 2 to 3). (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Hospitalizations are less likely among individuals receiving maintenance therapy with antipsychotics (NNT = 8; 95% CI, 6 to 14). (SOR: A, based on consistent, good-quality patient-oriented evidence.) People taking antipsychotic drugs are more likely to experience adverse effects, including movement disorders (number needed to harm [NNH] = 20; 95% CI, 14 to 50) and weight gain (NNH = 25; 95% CI, 20 to 50).1 (SOR: A, based on consistent, good-quality patient-oriented evidence.) Schizophrenia is the most common psychotic disease, with an estimated prevalence of 0.25% to 0.64% in the U.S. population.2 Given the limited access to psychiatrists in many parts of the country, family physicians are often called on to screen, diagnose, and treat a variety of psychiatric conditions, including schizophrenia.3,4 In particular, family physicians may be in a position to counsel patients and families on the benefits and risks of continuing antipsychotic medications for the treatment of schizophrenia. This Cochrane review aimed to answer questions about whether maintaining antipsychotic therapy prevented relapse of schizophrenia symptoms, reduced hospitalizations, improved quality of life and social functioning, or was associated with adverse effects. The Cochrane review included 75 randomized controlled trials involving 9,145 patients with schizophrenia or schizophrenia-like illness and compared those taking antipsychotic medications with those taking placebo.1 The included trials were published between 1959 and 2017. The primary outcome was whether antipsychotic drugs were effective at preventing relapse of psychotic symptoms among individuals with schizophrenia or schizophrenia-like illness. The meta-analysis found that these medications were effective at preventing symptom relapse at seven to 12 months (NNT = 3; 95% CI, 2 to 3). Individuals receiving antipsychotic drugs were also less likely to be hospitalized compared with those taking placebo (NNT = 8; 95% CI, 6 to 14). Quality of life and social functioning may be better for patients receiving antipsychotics, based on low- and moderate-certainty evidence, respectively. No statistically significant differences were identified between groups for likelihood of employment or death from suicide. Individuals receiving antipsychotic drugs were more likely to experience movement disorders (NNH = 20; 95% CI, 14 to 50) and weight gain (NNH = 25; 95% CI, 20 to 50). In both cases, the rate of adverse effects associated with the antipsychotic medication increased over time, with no statistically significant differences identified during the first three months of treatment. There was a trend toward increased sedation among those treated with antipsychotics vs. placebo, but the difference was not statistically significant. A practice guideline from the American Psychiatric Association recommends that patients with schizophrenia whose symptoms have improved with antipsychotic use continue treatment. It also states that when antipsychotic drugs are administered on a long-term basis, adverse effects such as movement disorders and weight gain are common. For this reason, the American Psychiatric Association recommends preventive interventions such as early intervention for weight gain and regular screening for lipid and glucose abnormalities. Similarly, patients should be monitoring for movement disorders, with a continual discussion around benefits and adverse effects associated with the medications in the context of shared medical decision-making.4 Editor's Note: Dr. Salisbury-Afshar is a contributing editor for AFP. Page 5 Are educational, supportive, behavioral, or mixed intervention strategies effective at increasing compliance with continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA)? Behavioral interventions increase CPAP use (mean difference [MD] = 1.31 hours per night; 95% CI, 0.95 to 1.66) compared with usual care. These interventions also increase CPAP adherence, measured by participants using their machine four or more hours per night, from 371 to 501 per 1,000 patients (number needed to treat [NNT] = 8; 95% CI, 5 to 23). Supportive interventions may slightly increase CPAP use (MD = 0.70 hours per night; 95% CI, 0.36 to 1.05) vs. usual care, and they increase CPAP adherence from 601 to 717 per 1,000 patients (NNT = 9; 95% CI, 5 to 56). The benefits of educational and mixed interventions are unclear because of low-quality evidence.1 (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.) OSA causes sleep fragmentation and can lead to excessive daytime sleepiness, mood changes, and impairments in cognition, memory, and driving competence. OSA increases the risk of cardiovascular, cerebrovascular, and metabolic morbidity.2 CPAP is first-line treatment for OSA, and consistent use can improve sleep quality and associated symptoms.3 A large systematic review and meta-analysis showed that CPAP had no effect on cardiovascular outcomes in patients with OSA; however, in most randomized controlled trials, patients used CPAP less than four hours per night.4 The effectiveness of CPAP on OSA symptoms directly correlates to duration of compliance, with more than four hours of adherence to therapy demonstrating improvements in sleep quality, daytime sleepiness, fatigue, and depressive symptoms.5 This Cochrane review included 41 studies with 9,005 participants.1 It evaluated the effectiveness of educational, supportive, behavioral, and mixed interventions on CPAP compliance compared with usual care, which was defined as providing background information and general instructions for CPAP use.1 Most participants were CPAP naive. Educational interventions aimed to improve patient knowledge and understanding of OSA in general or CPAP treatment specifically and were delivered in various formats (written, group, video, in-person). Supportive interventions used automated feedback from the CPAP machine that triggered a clinician intervention or scheduled a follow-up visit to encourage CPAP use. Behavioral interventions included motivational enhancement therapy, social cognitive theory, transtheoretical/stages of change model, and cognitive behavior therapy to improve compliance. Mixed interventions were any combination of the previous interventions. The authors used total CPAP hours per night and total number of participants who used the machine four or more hours per night to measure CPAP compliance. Patient-oriented outcomes of daytime sleepiness and quality of life could not be evaluated because of inconsistency in measurement among studies. Based on high-certainty evidence, behavioral interventions demonstrated a significant benefit (MD = 1.31 more hours per night of CPAP use compared with usual care; 95% CI, 0.95 to 1.66). They also increased the number of participants adhering to therapy, assessed by using their machine for four or more hours per night, from 371 to 501 per 1,000 (NNT = 8; 95% CI, 5 to 23). Patients using behavioral interventions were less likely to withdraw from therapy based on a decrease in study withdrawals from 146 to 101 per 1,000 (NNT = 22; 95% CI, 13 to 33). Supportive interventions increased CPAP use (MD = 0.70 hours per night; 95% CI, 0.36 to 1.05) and increased adherence to therapy from 601 to 717 per 1,000 participants (NNT = 9; 95% CI, 5 to 56) compared with usual care, although these results were based on moderate- and low-certainty evidence, respectively. The benefits of educational and mixed interventions to improve CPAP compliance were uncertain due to low-quality evidence. This Cochrane review supports the use of behavioral interventions to improve CPAP compliance. Although the studies used various behavioral intervention techniques, the key concept is to engage or interact with the patient in some way. The American Academy of Sleep Medicine strongly recommends educational interventions and conditionally recommends behavioral and troubleshooting (similar to supportive) interventions.3 The Department of Veterans Affairs/Department of Defense clinical practice guideline also includes recommendations for educational, behavioral, and supportive interventions to improve adherence to CPAP therapy in patients with OSA.6 Both guidelines recommend using these interventions during the initiation phase of CPAP therapy.3,6 Editor's Note: The NNTs and CIs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review. The views expressed in this article are those of the authors and do not

necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the U.S. government. I am a military service member. This work was prepared as part of my official duties. Title 17 U.S.C. 105 provides that "Copyright protection under this title is not available for any work of the United States Government." Title 17 U.S.C. 101 defines U.S. government work as a work prepared by a military service member or employee of the U.S. government as part of that person's official duties. Page 6 Onychomycosis, a chronic fungal infection of the fingernail or toenail bed, is commonly encountered in primary care. Onychomycosis is not just a cosmetic problem. If untreated, it can cause pain, discomfort, and physical impairment, negatively impacting quality of life. This article provides a summary of the best available patient-oriented evidence on the diagnosis and management of this condition. The estimated point prevalence of onychomycosis in North America is up to 13.8% for adults and 0.44% for children and adolescents younger than 18 years.1,2 Age older than 60 years is an important risk factor because of poor peripheral circulation, suboptimal immune function, slower nail growth, and longer exposure to pathogenic fungi.3 Other risk factors include recurrent nail trauma, tobacco use, and certain comorbidities (diabetes mellitus, obesity, psoriasis, malignancy, HIV, peripheral vascular disease, immunocompromised state). Dermatophytes cause 70% of onychomycosis infections in the United States, with the remaining 30% caused by nondermatophyte molds and yeasts.4 One study showed that 39% of infections were mixed (caused by dermatophytes plus nondermatophyte mold and/or yeast), making diagnosis and treatment challenging.5 DIFFERENTIAL DIAGNOSIS AND CLINICAL PRESENTATION With fungi causing 50% of nail dystrophies, the differential diagnosis for nail abnormalities is large (Table 1).6–10 Common signs and symptoms of onychomycosis include nails that appear discolored (Figure 1), deformed (Figure 2), hypertrophic, or hyperkeratotic; subungual debris; separation from the nail bed; brittle nails that break easily or crumble (Figure 3); and nails that are foul smelling.Onychomycosis is classified into several subtypes based on the phenotypic pattern of nail invasion (Table 2).8,11,12 Severity is classified as mild, moderate, or severe based on the Onychomycosis Severity Index. This index uses three clinical features to assess severity: area of involvement, proximity of disease to the nail matrix, and presence of dermatophytoma or subungual hyperkeratosis thickness greater than 2 mm.13 Laboratory confirmation of nail infection is important for accurate diagnosis.14 A potassium hydroxide (KOH) preparation with direct microscopy is the preferred diagnostic method because it is highly specific, has rapid results, and is cost-effective.12,15 Diagnosis by KOH preparation alone is sufficient for treatment initiation. However, if KOH results are negative and there is high clinical suspicion for onychomycosis, other testing may be performed to confirm the diagnosis. Table 3 includes the accuracy of diagnostic testing methods.16,17 Fungal culture of nail clippings or subungual debris allows for species differentiation but is limited by cost and the time it takes to get results. Biopsy and periodic acid–Schiff stain of nail clippings can help assess the degree of nail plate involvement. Polymerase chain reaction can also confirm the diagnosis but is more expensive than other tests.15–17 Because samples should be taken from the most proximal area of onycholysis (Figure 4), the nail plate may need to be trimmed to reveal this area.Diagnostic testing is generally recommended before initiating treatment, but empiric treatment with terbinafine can be considered if testing is cost prohibitive.18 INDICATIONS FOR MEDICAL THERAPY Indications for oral and topical therapy are listed in Table 4.12,19 Shared decision-making based on disease severity, length of treatment, cost, comorbidities, risk of drug-drug interactions, adverse effects, and patient preference should be used before initiating treatment. The type of treatment depends on clinical features and the degree of nail involvement.Onychomycosis can have a significant impact on quality of life and will progress if left untreated.20 Oral therapy is the most effective treatment for onychomycosis of any severity.21 Oral antifungals have higher cure rates and shorter treatment periods than topical therapy (Table 5).19,22–31 Terbinafine is the most effective oral agent based on its high clinical cure rate (complete nail clearance) and mycologic cure rate (negative microscopy and culture results) and should be recommended as first-line therapy.21–24 Terbinafine is less expensive than topical agents. Chronic or active liver disease is the main contraindication to terbinafine use because of reports of mild and severe liver injuries. The U.S. Food and Drug Administration (FDA) recommends transaminase testing before initiating terbinafine therapy. Subsequent laboratory monitoring is not necessary for immunocompetent patients.32 Drugs that may interact with concomitant terbinafine therapy include tricyclic antidepressants, selective serotonin reuptake inhibitors, tamoxifen, atypical antipsychotics, and beta blockers.Continuous itraconazole (Sporanox) therapy is FDA approved for toenail onychomycosis, and a pulse-dosing regimen (i.e., interval treatment cycles) is approved for fingernail onychomycosis. According to a five-year double-blind prospective study with 144 patients, mycologic and clinical relapse rates are significantly higher with itraconazole than with terbinafine in patients who have severe disease (53% vs. 23% and 48% vs. 21%, respectively; P < .001).24 A systematic review and network meta-analysis of 22 trials (n = 4,205) using oral antifungal agents for toenail onychomycosis showed that terbinafine is likely more effective than itraconazole in achieving complete cure.33 Fluconazole (Diflucan), 150 mg weekly for at least six months for fingernails and toenails, may be used as an off-label alternative treatment if the patient is unable to tolerate terbinafine or itraconazole.27,28,31 Griseofulvin is rarely used because of long treatment duration, higher risk of adverse events, and lower cure rates compared with other medications.34 A systematic review comparing continuous or pulse-dosing oral antifungal regimens for the treatment of toenail onychomycosis found no significant differences in effectiveness and safety.33 There are no systemic therapies approved by the FDA for the treatment of onychomycosis in children, although terbinafine and itraconazole are considered off-label treatments.35 Topical therapy can be used in children if there are three or fewer nails involved, less than 50% of the nail plate surface area is affected with no matrix involvement, or oral therapy is contraindicated.36 It is important for clinicians to counsel patients about realistic expectations for complete cure because fingernails typically take three to six months to completely regrow and toenails can take up to 18 months. Although topical therapy is less effective and more expensive than oral therapy, it can be used as an alternative first-line treatment in patients with superficial onychomycosis or early distal lateral subungual onychomycosis because of low risks of adverse effects and minimal drug-drug interactions.19,37,38 The recommended duration of topical therapy is 24 weeks for fingernails and 48 weeks for toenails.12 Adverse effects are generally limited to exfoliation, erythema, burning, and dermatitis at the application site.39 Ciclopirox 8% topical solution is FDA approved for mild to moderate fingernail and toenail onychomycosis. Two randomized controlled trials (RCTs) including 460 total patients showed that compared with vehicle, ciclopirox 8% is better at achieving complete cure at 48 weeks, although only the second study was statistically significant (study 1: 5.5% vs. 0.9%; P = .059 and study 2: 8.5% vs. 0%; P = .001).29 Once-daily treatment with efinaconazole 10% (Jublia) is an option for mild to moderate onychomycosis. In two phase 3 randomized studies including 1,655 total patients with moderate disease, complete cure rates were higher with efinaconazole 10% compared with vehicle (17.8% vs. 3.3%; P < .001; number needed to treat [NNT] = 7 in study 1 and 15.2% vs. 5.5%; P < .001; NNT = 10 in study 2).40 In two phase 2 randomized studies including a total of 1,198 patients with moderate disease, tavaborole 5% (Kerydin) had favorable effectiveness compared with ciclopirox, although, again, absolute treatment benefit is low. Complete cure rates compared with vehicle were 6.5% vs. 0.5% (P < .001; NNT = 17) in study 1 and 9.1% vs. 1.5% (P < .001; NNT = 13) in study 2. 41 Amorolfine 5% lacquer (not available in the United States) can be used for onychomycosis without matrix involvement and for mild distal lateral subungual onychomycosis (Figure 5) that affects up to two nails. A small RCT with 24 patients showed a mycologic cure rate of 8% (P < .001) with once-weekly treatment for nine months.42 Nail trimming and debridement can be used with oral or topical pharmacologic therapy to increase treatment effectiveness. Surgical and nonsurgical nail removal may be indicated for severe infection or when medical therapy fails.Dual-wavelength infrared and fractional carbon-dioxide laser therapy are FDA approved for temporary cosmetic improvement of nails based on low-level evidence and small RCTs.43,44 Combining laser therapy with topical therapy increases overall treatment effectiveness.45 Tea tree oil, oregano, vitamin E, oil of bitter orange, vinegar sock soaks, and menthol-camphor ointment (Vicks VapoRub) have demonstrated antifungal activity in small-scale studies.46–49 More robust studies are needed to evaluate the effectiveness of these essential oils against onychomycosis.50,51 Although photodynamic and plasma therapies have been explored for the treatment of onychomycosis, larger randomized trials are needed to determine their effectiveness and feasibility for use in the clinical setting.4 Plasma therapy creates air using pulses of strong electric field that ionize air molecules, generating ozone, hydroxyl radicals, and nitric oxide, which have antifungal properties. A pilot study of 19 participants without a control group showed an overall clinical cure rate of 53.8%.52 Photodynamic therapy is a noninvasive treatment that combines light-based modalities with photosensitizers. It has been used as an off-label treatment for onychomycosis. A double-dummy RCT including 80 participants with confirmed fungal toenail onychomycosis compared biweekly photodynamic therapy with once-weekly fluconazole, 300 mg, for 24 weeks. Although response to treatment at 24 weeks was greater with photodynamic therapy (90% vs. 40%; P = .002; NNT = 2), this was not a blinded study.53 The relapse rate of onychomycosis is 20% to 25%, with the condition likely to recur within two years of successful therapy.54 Features associated with poor prognosis include age older than 70 years, history of nail trauma, and diabetes.4 Based on expert opinion, avoiding walking barefoot in public places may help prevent recurrence.55 Patients should disinfect shoes and socks, keep feet cool and dry, and recognize the early signs of recurrence and reinfection.56 Immediate treatment of tinea pedis can also delay onychomycosis recurrence because the infected skin can act as a reservoir of infection.57 Compared with no prophylaxis, twice-weekly prophylaxis with a topical antifungal following terbinafine treatment has been shown to decrease the rate of recurrence (33% vs. 76%; P < .001).58 Data Sources: A PubMed search was completed in Clinical Queries using the key terms onychomycosis, tinea unguium, and nail fungus. The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. Also searched were the Cochrane database, DynaMed, and Essential Evidence Plus. Search dates: November 13, 2020, and August 15, 2021. Page 7 Hepatitis A is a common cause of acute hepatic inflammation and jaundice worldwide, and until 2004 it was the most commonly reported type of hepatitis in the United States.1 A combination of widespread vaccination, food safety practices, and improved sanitation decreased the incidence of hepatitis A in the United States from the 1970s until 2015. However, infection rates have recently increased because of large community outbreaks in susceptible individuals.2 Worldwide, an estimated 1.4 million cases of hepatitis A are reported each year, and it remains a major infectious disease for most of the world's population.3 Before the development and implementation of the hepatitis A vaccine, annual cases of acute infection in the United States were reported in the tens of thousands, peaking at 59,606 cases in 1971.4 Following the licensing of the first vaccine, the annual number of U.S. cases fell by 92% between 1995 and 2010.1 This decline in cases occurred after only moderate vaccination coverage was achieved, indicating a substantial herd immunity effect.5 However, the United States has seen a steep increase in cases, driven by several person-to-person and food-related outbreaks beginning in 2016.4,6,7 These episodes, along with several outbreaks in Europe over the past five years, have led to resurgences of hepatitis A in areas considered low-endemic regions.3,8 The lack of widespread adult immunity in the affected nations, whether due to poor immunization rates or few previous infections, provides fuel for outbreaks.9 Advances in virus genotyping have allowed researchers to track outbreak origin and trajectory.10 Transmission and Risk Factors Hepatitis A virus is a nonenveloped positive-strand RNA virus classified as a picornavirus, whose only natural host is humans.1 Remarkably stable in many environments and able to survive on surfaces for weeks, hepatitis A virus is transmitted through ingestion of infected stool particles.11–13 The virus is absorbed in the stomach and intestines, travels to the liver via the portal circulation, and replicates in hepatocytes.11,12 Detectable virus appears in blood and feces approximately 10 to 12 days after infection and may be excreted in stool for up to three weeks after the onset of symptoms.1,12 Viral shedding may begin weeks before symptom onset, contributing to the scope of outbreaks.4,12 Close interpersonal or sexual contact with an infected person and consumption of contaminated food or water are the most common routes of infection.4,14 Less commonly, infection has resulted from injection drug use or blood transfusion.4,12,14 Risk factors for contracting hepatitis A and characteristics that increase the risk of complications from infection are listed in Table 1.2 Presentation and Complications An incubation phase of approximately 30 days (range = 15 to 50) is followed by the development of infectious symptoms in most adults and children six years and older.4,12 Approximately 70% of children younger than six years remain asymptomatic.4 Patients often initially experience nonspecific flulike symptoms of fever, malaise, nausea with vomiting, and abdominal pain that may progress to the classic findings of dark urine and jaundice in 70% of adults and older children.4,12 Although less common, diarrhea, joint pain, pruritus, and skin eruptions may also occur.12 Hepatomegaly and jaundice are the most common examination findings, occurring in 78% and 40% to 80% of patients, respectively.12 Patients with hepatitis A are most likely to spread the disease in the 14 days before jaundice develops, corresponding with the highest level of the virus in the stool.15 Infectivity decreases after jaundice is observed, and most individuals are considered to be noninfectious one week after the onset of jaundice.15 Most cases of acute hepatitis A are self-limited. Unlike other types of viral hepatitis, hepatitis A is not a chronic disease. However, approximately 10% to 15% of patients may take up to six months to fully recover or may have recurrent symptoms during this time frame.12 Occurring in less than 1% of patients, acute liver failure is more likely in patients who are older than 40 years at the time of infection and in those with underlying liver disease.12,16 Rare but serious extrahepatic manifestations have been reported, including acute renal failure, transverse myelitis, Guillain-Barré syndrome, pancreatitis, cholecystitis, reactive arthritis, anemia, and pleural or pericardial effusion.12,16–18 Pregnant patients who develop hepatitis A are at increased risk of complications such as preterm contractions, placental separation, and premature rupture of membranes, increasing the likelihood of preterm labor and delivery.19 The diagnosis of hepatitis A cannot be made solely on clinical grounds.1 Laboratory findings in symptomatic patients may include elevations of serum transaminase levels (with the alanine transaminase level higher than the aspartate transaminase level), total and direct bilirubin, and alkaline phosphatase, which may take two to three months to resolve.12,15,17 In cases of severe symptoms, further testing may include a complete blood count, prothrombin time, serum electrolytes, and glucose level; a creatinine level greater than 2 mg per dL (176.8 μmol per L) is a positive predictor of fulminant hepatitis and death.12 No nonspecific laboratory findings are diagnostic of hepatitis A.2 Similarly, although epidemiologic factors may suggest hepatitis A, serologic testing is required to confirm the diagnosis.2,4 Immunoglobulin M (IgM) anti–hepatitis A antibodies generally become detectable five to 10 days before the onset of symptoms, peak within one month of illness, and can persist for more than six months.15 Testing is recommended only for symptomatic patients with suspected hepatitis A. IgG anti–hepatitis A antibodies appear during the convalescent phase, remain elevated throughout a patient's lifetime, and indicate enduring protection against hepatitis A; unimmunized patients who are IgM anti–hepatitis A negative but IgG anti–hepatitis A positive are considered to have evidence of past infection and recovery.15 Total anti–hepatitis A contains measurements of both IgM and IgG, and it can be used to identify unimmunized patients who are immune because of previous hepatitis A.2 Molecular virology methods may be useful in the investigation of common-source outbreaks of hepatitis A but are not necessary for routine clinical diagnosis.2 The expected laboratory findings and clinical course of acute hepatitis A are represented in Figure 1.20 There is no specific treatment for hepatitis A.2 Relative rest, oral rehydration, and treatment of symptoms such as nausea, vomiting, and diarrhea are recommended. Hepatotoxins, including acetaminophen and alcohol, should be avoided. If fulminant hepatic failure develops, characterized by acute mental status changes or new coagulopathy, liver transplantation may be considered. Vaccination with inactivated hepatitis A antigen is the primary approach to preventing acute infection in the United States. There are two single-antigen vaccines (Havrix and Vaqta) and a combination vaccine (Twinrix) that contains Havrix and hepatitis B viral antigen (Table 2).21 Vaccine effectiveness is reported at 94% for Havrix (two doses) and 100% for Vaqta (one dose) four weeks after immunization.2 Long-term data following the completion of a two-dose series of both Havrix and Vaqta suggest lifelong immunity with this immunization schedule.2 Single-dose immunization is not recommended in the United States.2 Hepatitis A vaccines can be administered concurrently with other vaccines.2 Routine vaccination is recommended for children 12 to 23 months of age and for other high-risk populations2 (Table 12). The Advisory Committee on Immunization Practices recommends vaccination for any pregnant patient with an indication for vaccination and for any patient who requests immunization.2 Vaccination is not routinely recommended for health care workers, sewer workers, plumbers, or child care workers.1 Administration of immune globulin (Gama-stan) provides passive immunization by introduction of anti–hepatitis A antibodies.2 Although it can be given simultaneously with inactivated vaccines administered at different sites, the manufacturer recommends that the measles-mumps-rubella and varicella virus vaccines be given two weeks before or six months after immune globulin.2 Potential adverse effects of immune globulin include hypersensitivity reactions and an increased risk of thrombosis,22 and it is more expensive than available vaccines.23,24 Unlike with the hepatitis A vaccine, the protection provided by immune globulin is limited to approximately three months.2 Pre-exposure prophylaxis is indicated for unimmunized patients who are planning to travel to an area with an increased incidence of hepatitis A, which is considered to be everywhere outside of the United States except for Australia, Canada, Japan, New Zealand, and western Europe.2 In general, all otherwise healthy children younger than six months and persons with an allergy to the hepatitis A vaccine should receive immune globulin instead. Persons older than 40 years and those older than six months who are immunocompromised or have chronic liver disease should receive both the vaccine and immune globulin. All other individuals should receive hepatitis A vaccine only (Table 3).2 Postexposure prophylaxis is recommended for all unvaccinated individuals with significant exposure in the previous two weeks, including sex partners, household contacts, or known contaminated food sources.2 Immune globulin should be given only to children younger than 12 months and those in whom the vaccine is contraindicated, such as someone with an allergy to neomycin or another component of the vaccine.2 Both the vaccine and immune globulin are recommended for adults older than 40 years and children older than 12 months who are immunocompromised or have chronic liver disease. All other patients should receive a single dose of hepatitis A vaccine (Table 4).2 In the event of a community outbreak, public health officials should help to coordinate an effective postexposure prophylaxis strategy. Data Sources: We conducted literature searches using Ovid, PubMed, the Cochrane database, Essential Evidence Plus, and the U.S. Preventive Services Task Force database, focusing on the keywords hepatitis A and hepatitis A immunization. Search dates: October 2020 through May 2021. Page 8 Bioterrorism is the deliberate release of viruses, bacteria, toxins, or fungi with the goal of causing panic, mass casualties, or economic disruption.1 Historical records indicate that biological warfare has occurred throughout history, as long ago as the 14th century B.C.2 Although many pathogens may be used in a bioterrorist attack, the most concerning agents to national security and public health are anthrax, smallpox, plague, tularemia, botulism, and viral hemorrhagic fevers, in descending order of likelihood1 (Table 13). These pathogens are considered category A agents by the Centers for Disease Control and Prevention (CDC) and are the focus of this article. Although bioterrorism is currently considered a low-probability event, many pathogens that could be used in bioterrorist attacks occur naturally. Five of the category A agents—anthrax, botulism, plague, Ebola virus, and Lassa fever—were noted to occur naturally in endemic regions in 2020.4 There is also concern that these (or other) pathogens could be altered to increase virulence or cause resistance to current medications and vaccines.5 Laboratory accidents have resulted in the release of harmful pathogens, and the shipment of viable agents and unaccounted stocks of these agents highlight the risk of poor biosecurity.2,6,7 An emerging infectious disease, such as a novel respiratory virus, might also be exploited, bypassing the expertise needed to obtain and weaponize other well-known agents. In 1975, all but 12 nations participated in the Biological Weapons Convention, which prohibited the development, production, acquisition, use, and stockpiling of biological agents.8 Despite this, from 1981 to 2018, there were 37 bioterrorist attacks worldwide.9 In 2001, powdered anthrax spores were mailed through the United States Postal Service to several government employees and news media outlets. This attack resulted in 11 cutaneous and 11 inhalational cases of anthrax, with five of the inhalational cases being fatal.1,10 An estimated $320 million was needed for decontamination, and 10,000 people were recommended for postexposure prophylaxis.11,12 In 2020, ricin (a poison found in castor beans) was mailed to the President of the United States and five residents of Texas.13 Ricin can cause death within 36 to 72 hours, and there is no known antidote.14 The initial diagnosis of illness caused by biological agents could be delayed because of a lack of clinical experience with or knowledge about these agents.15 The goal of this article is to provide primary care physicians with basic information about category A agents, supporting them in detecting and responding to a bioterrorist attack, which may include assisting in a mass casualty event.15,16 Primary care physicians may be the first to recognize a bioterrorism-related illness by noting an unusual presentation, location, timing, or severity of disease. Anthrax is a naturally occurring zoonotic disease with worldwide distribution caused by the spore-forming, gram-positive, rod-shaped bacterium, Bacillus anthracis.17 Although anthrax is a disease primarily affecting wild and domestic herbivores, it occasionally causes human illness and is potentially fatal. The human disease has a variety of manifestations. Cutaneous disease is most common, but anthrax that is inhaled possesses a higher degree of lethality.18 The inhalational form is of concern to bioterrorism because it is easily disseminated and can cause widespread illness and death.2,19 For instance, an aerosolized release of anthrax into the Washington, DC area could result in 1 million to 3 million deaths.16 The median incubation period for anthrax in the 2001 attack was four days, but incubation may extend for up to two months postexposure.19 The initial presentation of inhalational anthrax is difficult to distinguish from other common illnesses such as community-acquired pneumonia, seasonal influenza, or COVID-19. Symptoms are constitutional and include fevers, chills, lethargy, and cough. The mortality rate of naturally occurring inhalational anthrax is 30% to 45%, and refined spores, which would likely be used in a malicious attack, would be even more lethal.17,19 Anthrax disease can be confirmed with laboratory diagnostic testing such as a Gram stain or polymerase chain reaction (PCR) testing. The historical test of choice is a bacterial culture. Following exposure to aerosolized anthrax spores, the CDC recommends a postexposure regimen of 60 days of antimicrobial prophylaxis (Table 2).20 The optimal postexposure treatment regimen combines antibiotics with three doses of anthrax vaccine21 (Table 322–25). Treatment for active illness involves antimicrobial therapy with the administration of anthrax antitoxins or monoclonal antibodies.26 There are currently two monoclonal antibodies and one antitoxin approved by the U.S. Food and Drug Administration (FDA): raxibacumab (Abthrax), obiltoxaximab (Anthim), and anthrax immune globulin intravenous (Anthrasil).26 These agents should be administered in consultation with regional medical authorities and the CDC. Smallpox is caused by the variola virus and has led to an estimated 300 million deaths in the past century.20 In 1979, the virus was declared eradicated by the World Health Organization, and the last naturally occurring case of infection was documented in 1977.27 Smallpox infection has two forms: the more lethal variola major and the milder variola minor. Transmission is primarily via the respiratory tract, and person-to-person transmission is the most common. Smallpox is one of the highest-threat biological agents because it is highly contagious, and only 100 infected individuals could cause a pandemic.15 The historical fatality rate of smallpox is between 30% and 50% in an unvaccinated population.28 Current modeling of aerosolized smallpox suggests a higher fatality rate if it were released today.27,29 Routine vaccination against smallpox in the United States ended in 1972, and people who were vaccinated before that date have unknown immunity.30 Following a 12- to 14-day incubation period, smallpox presents with high fevers, vomiting, headaches, myalgias, and malaise. This initial phase is closely followed by a characteristic rash on the face, forearms, and mucous membranes of the oropharynx. The rash is initially maculopapular, but the pathognomonic rash has deep-seated, rigid vesicles in the same stage of development (Figure 131). Involvement of the palms and soles is also typical. Infection must be confirmed in a CDC-certified laboratory using approved PCR testing protocols. Vaccine prophylaxis is an option to prevent or reduce severity, but it is only applicable if administered before symptom onset, ideally within four days of exposure.32 Fetal vaccinia has been reported after smallpox vaccination of pregnant patients; therefore, the vaccine should not be administered during pregnancy unless benefits are thought to outweigh risks. In 2018, the FDA approved tecovirimat (TPOXX) for the treatment of smallpox.33 Although limited clinical data are available, tecovirimat, which interrupts virus transmission between cells, has been used to treat severe vaccinia.34 The antiviral agents cidofovir and brincidofovir have also shown effectiveness against other orthopoxviruses. Pregnant patients should receive similar treatment after exposure. Reluctance to treat may lead to adverse outcomes. Plague is caused by the gram-negative bacterium Yersinia pestis.35 The most common form is bubonic plague, which occurs after the bite of an infected flea. Clinical features include fever and painfully swollen lymph nodes called buboes. Pneumonic plague is less common but highly contagious because it is spread from person to person. The pneumonic plague has a case-fatality rate approaching 100% in the absence of effective treatment. A productive cough with bloody sputum defines the pneumonic form.15 The pneumonic plague is the greatest threat as an agent of bioterrorism, with an aerosolized release resulting in many primary pneumonic plague cases.15 The incubation period is typically one to six days. The bacterium can be isolated directly from bubo aspirates and cultured from sputum, tracheal aspirates, or blood. Additional diagnostic techniques include PCR testing and culture methodologies because the bacterium grows well on standard media. Following exposure to the plague, postexposure prophylaxis is indicated and often consists of a seven-day course of antibiotics (Table 220). Antimicrobial therapy is effective for treating the full spectrum of the illness.36 Tularemia is a zoonotic disease caused by the bacterium Francisella tularensis. This pathogen has a geographic distribution throughout North America.37 It has many natural reservoirs, with domestic rabbits serving as the primary source of human infection through direct contact. Tularemia can present in many forms, from asymptomatic to symptoms of severe disease and death; however, the pneumonic form is the biggest threat as a biological weapon because an aerosolized dispersal could result in a large number of pleuropneumonia cases.37 Diagnosis is confirmed with fluorescent antibody testing, immunohistochemical staining, or PCR testing of tracheal or blood samples. Treatment involves the use of selected antimicrobial agents38 (Table 220). Isolation is generally not recommended because of the lack of person-to-person transmission (Table 420). Laboratory personnel should be alerted when tularemia is suspected or exposure is known. Botulism is caused by the toxin produced by Clostridium botulinum, a spore-forming bacterium that occurs naturally in soil. The toxin has potent neuroparalytic effects.39 By mass, the botulinum neurotoxin is the most poisonous substance known. Botulism is characterized by neuroparalytic signs, typically starting with cranial nerve involvement that presents as diplopia, dysphagia, and dysarthria in an afebrile patient. A progressive, bilateral, descending motor neuron flaccid paralysis then follows, resulting in respiratory failure and death.40 Most natural illnesses related to botulinum toxin occur because of improper food storage (canning or pickling) or as the result of under-cooked food.41 The most likely bioterrorism scenarios include intentional contamination of foodstuffs or aerosolization of the bacterium. Laboratory confirmation is achieved by finding botulinum toxin in stool or blood or by culturing C. botulinum directly. The most widely used agent is botulism antitoxin heptavalent (A, B, C, D, E, F, G - equine). Administration of antitoxins does not reverse paralysis but halts further progression42; therefore, early administration is crucial.43 Obtaining the antitoxin for infants and adults requires consultation with your state health department and subsequent consultation with and distribution of the antitoxin from the CDC. Initiation of the process should not be delayed while awaiting formal confirmation of disease.44,45 Viral hemorrhagic fevers of importance to humans are caused by viruses that are members of the Filoviridae and Arenaviridae families.46 Category A agents include the geographically dispersed Lassa, Ebola, and Marburg viruses, and the Machupo virus that is endemic in South America. Bats and rodents are typically the suspected reservoirs for Filoviridae and Arenaviridae, respectively. Naturally occurring viral hemorrhagic fevers are contracted through direct contact with bodily fluids. In a bioterrorist attack, aerosolization is the most likely mode for dissemination.47 Incubation ranges from two to 21 days, followed by abrupt onset of fevers, myalgia, headaches, vomiting, abdominal pain, and diarrhea.48 Late-stage manifestations include hepatic failure, renal failure, hemorrhagic diathesis, shock, and multiorgan dysfunction. Diagnosis focuses on antigen detection assays or PCR testing of blood samples. Direct virus isolation is also an option. Isolation of patients suspected of having a viral hemorrhagic fever is essential, and treatment has focused on supportive measures. In recent years, progress has been made in the treatment of Ebola disease. Several new FDA-approved treatments exist (Table 220). Monoclonal antibody treatments are under evaluation, notably atoltivimab/maftivimab/odesivimab (Inmazeb) and ansuvimab (Ebanga). Both therapies have demonstrated benefit when administered to patients with Ebola hemorrhagic fever.49 Preparing for a Bioterrorist Attack TRAINING AND INFECTION CONTROL Mass casualty and disaster management are not routinely included in medical school or residency curricula.50,51 A national survey of 1,603 physicians found that only one-third of respondents reported feeling comfortable about their ability to manage public health emergencies such as bioterrorist attacks, and only one-half had participated in emergency training during the previous two years.52 Training resources are available (Table 5). The American Academy of Family Physicians provides resources for personal, practice, and community preparedness. The U.S. Department of Homeland Security has a comprehensive list of training resources on bioterrorism and disaster preparedness. The U.S. Army offers didactics on the medical management of biological weapon casualties and free downloadable guides on bioterrorism.20,53 There are also volunteer and training opportunities for clinicians interested in disaster management.54,55 In the event of a bioterrorism incident, infection control and contact tracing will be important to mitigate an outbreak effectively and will likely focus on isolating affected individuals.56 The availability of personal protective equipment will need to be maximized. Established routes of communication with local public health departments will be important for establishing and refining disaster protocols. Clinicians should be familiar with the treatment of children and pregnant patients because a bioterrorist attack would likely affect broad segments of the population.57 Routine vaccinations should be maintained as outlined by the CDC.55 However, immunizations for potential biological agents are not regularly administered, except to high-risk groups such as military personnel and laboratory workers (Table 322–25). Vaccination for smallpox, anthrax, and Ebola disease should be considered for people at high risk of exposure.23 There are two smallpox vaccines: ACAM2000 and Jynneos.23,24 An anthrax vaccine (BioThrax) is approved for pre- and postexposure prophylaxis.22 The Ervebo vaccine for Ebola Zaire was approved in 2019 for people 18 years and older.25 Vaccination for tularemia, plague, and botulism is not available in the United States. Microorganisms can be transported globally in a short amount of time. Examples included Severe Acute Respiratory Syndrome in 2003, Ebola disease in 2014, Middle East Respiratory Syndrome Coronavirus in 2015, and SARS-CoV-2 in 2019. It may be difficult to distinguish emerging infections from a bioterrorism event. An infectious agent that is genetically manipulated or not endemic may suggest a bioterrorism event.58 When a bioterrorist attack is suspected, it is crucial to notify public health officials to allow for the mobilization of resources (Table 6). This article updates a previous article on this topic by O'Brien, et al.1 Data Sources: PubMed was searched using the key words evaluation, treatment, preparedness, surveillance, detection of bioterrorism, anthrax, plague, smallpox, tularemia, botulism, and viral hemorrhagic fevers. An Essential Evidence Plus summary on bioterrorism was reviewed. The search was limited to English-only studies published since 2008. References from articles identified by the search were used. Search dates: October 2020 and April 2021. The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army Service at large. Page 9 Diabetes-related foot infections form in approximately 40% of foot ulcers in patients with diabetes mellitus.1 Infections can rapidly progress to cellulitis, abscess formation, osteomyelitis, and necrotizing fasciitis. In 2016, diabetes-related foot infections contributed to more than 130,000 lower-extremity amputations in the United States.2 The five-year mortality rate following amputation is approximately 50%, exceeding the mortality rate of many cancers.3 Patients with diabetes and vascular compromise, peripheral neuropathy, and impaired immune function are at high risk of developing foot infections. The risk increases with deformities (e.g., bunions, hammer toe, Charcot foot) that result in high compressive forces in certain areas of the foot.4 Peripheral neuropathy causes the loss of protective sensation for pain and temperature and increases the risk of foot trauma and ultimately foot ulceration. Approximately 50% of patients with neuropathy are asymptomatic, making recognition of a patient with an ulcer difficult.5 When the skin ulcerates, an infection can develop rapidly because of circulatory compromise and an impaired immune response. Infection can spread rapidly to surrounding tissues, initially causing cellulitis and later more severe complications such as osteomyelitis and necrotizing fasciitis.6 The most commonly isolated organisms from diabetes-related foot infections are the gram-positive bacteria Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus agalactiae (i.e., group B Streptococcus), and Enterococcus species. Wounds infected by methicillin-resistant S. aureus (MRSA) occur in approximately 15% of cases and are more serious considering the virulence of MRSA and the limited number of treatment options.7 Gram-negative bacteria are common and isolated in more than one-half of samples, particularly the Enterobacteriaceae group and Pseudomonas aeruginosa.8 Anaerobes are present in about one-third of cultures. Bacteroides fragilis, Prevotella, Porphyromonas, and Clostridium species are the most common.9 Approximately 50% to 80% of infections are polymicrobial, which complicates treatment.10 Prompt diagnosis of a diabetes-related foot infection decreases the risk of morbidity and mortality. Family physicians should consider patient risk factors (e.g., presence of foot ulcers greater than 2 cm, uncontrolled diabetes, poor vascular perfusion, comorbid illness) when assessing for infection. Findings suggestive of infection include erythema, induration, tenderness, warmth, and drainage. The probe-to-bone test is an office maneuver that is 87% sensitive and 83% specific for osteomyelitis.11 A probe-to-bone test result is positive if insertion of a sterile and blunt metal instrument is met with hard or gritty resistance. An erythrocyte sedimentation rate greater than 70 mm per hour is also suggestive of osteomyelitis.4,6 Other causes of inflammation (e.g., gout, rheumatoid arthritis, trauma) should be clinically ruled out. Although an elevated white blood cell count can indicate a more severe infection, it is not often elevated with a diabetes-related foot infection. C-reactive protein and procalcitonin correlate better to soft tissue bacterial infections than erythrocyte sedimentation rate and white blood cell count.6 Routine superficial wound cultures should be avoided because of the high rate of contaminants; however, deep tissue cultures obtained using aseptic procedures (i.e., incision and drainage, debridement, and bone culture) help guide treatment.6,12 A negative MRSA nares culture reduces the likelihood that a diabetes-related foot infection is caused by MRSA. Studies have shown correlations with negative predictive values between 73% and 90%.13,14 Plain radiography should be the initial imaging test if osteomyelitis is suspected.6,15 Osteomyelitis can take weeks to appear on radiographs; therefore, magnetic resonance imaging (MRI) or computed tomography (CT) is warranted if a concern for osteomyelitis persists with normal radiography findings. MRI helps detect soft tissue involvement and identifies the spatial orientation of infection to guide surgical planning. CT is appropriate if MRI is contraindicated.15 Vascular assessment should be performed on presentation, and patients with nonpalpable pulses should be formally evaluated for arterial insufficiency.16 Approximately 10% to 40% of people with diabetes have peripheral arterial disease.17 An ankle-brachial index is a quick and affordable way to assess blood flow, but it can be inaccurate because of arterial calcification with diabetes.16,18 Transcutaneous oximetry or arterial duplex ultrasonography may improve the accuracy of the vascular assessment.17,19 For more urgent detection of arterial disease, magnetic resonance angiography with and without intravenous contrast media or a CT with intravenous contrast media is preferred. If a patient is unable to receive intravenous contrast media because of renal disease, duplex ultrasonography of the lower extremity or magnetic resonance angiography without contrast media are appropriate alternatives.20 In 2019, the International Working Group on the Diabetic Foot published an update to the grading severity scale for diagnosing and classifying the extent of diabetes-related foot infections. This scale is the most validated scoring system to grade the severity of the infection and is summarized in Table 1.6 The scale scores a foot ulcer from 1 to 4 (1 = uninfected, 2 = mild infection, 3 = moderate infection, 4 = severe infection) and an "(O)" may follow scores 3 or 4 to indicate osteomyelitis. Erythema from a diabetes-related foot infection does not have to be contiguous to a foot ulcer in the updated classification scheme. 6 Scores of 3 (odds ratio [OR] = 1.7) or 4 (OR = 2.5) are associated with increased amputation rates.21 Other validated tools include the Site, Ischemia, Neuropathy, Bacterial Infection, and Depth scoring system and the Wound, Ischemia, foot Infection scale, which help predict outcomes and guide decisions for surgical interventions.18,22 The Perfusion, Extent, Depth, Infection, and Sensation score is a validated scale to predict amputation and mortality at six months and is available as an online calculator (.23,24 Figure 1 shows an uninfected ulcer, and Figure 2 shows an infected diabetes-related foot ulcer. Clinicians choosing antibiotics to treat patients with a diabetes-related foot infection should consider local antimicrobial sensitivities, the severity of infection, patient factors (e.g., drug-drug interactions, drug-disease interactions, renal dysfunction, drug allergies), previous antibiotic response, and patient preference. It is unclear if any one antibiotic is superior for resolving an infection or safer than other antibiotics.25 Empiric antibiotic coverage for a mild infection should include S. aureus and S. agalactiae.6 Guidelines also recommend empiric coverage for MRSA. A negative MRSA nares culture may help clinicians de-escalate MRSA-specific coverage considering the high negative predictive value of this test.6,13,14 Empiric antibiotic coverage for gram-negative rods (including P. aeruginosa) and anaerobes is reserved for moderate or severe infections, recurrent infections, or infections with severe limb ischemia.6 Antibiotics used to treat diabetes-related foot infections are summarized in Table 2.26–28 Oral antibiotics are appropriate for individuals with mild infection and some moderate infections, whereas intravenous antibiotics are always needed initially for a severe infection, including individuals with osteomyelitis.4,6 After the infection improves on intravenous antibiotics, it is reasonable to switch to an oral antibiotic. Oral antibiotics can also be used for osteomyelitis after five to seven days of intravenous coverage if the oral regimen has a high bioavailability.6 The optimal duration of antibiotic therapy for a diabetes-related foot infection depends on how quickly the infection improves, the severity of infection, and patient factors (e.g., peripheral vascular disease, antibiotic adherence, adverse antibiotic effects).29 Most patients should receive one to two weeks of antibiotics; however, treatment could be extended to three to four weeks for slowly resolving infections.4,6 Antibiotics may be needed for only a few days if osteomyelitis is surgically treated with amputation. Guidelines have recommended four to six weeks of antibiotics if osteomyelitis is not treated surgically, but recent evidence suggests three weeks of therapy may be similar to six weeks.4,6,30 Topical antibiotics are commonly applied to dressings for the prevention and treatment of mild diabetes-related foot infections. Resolution of a foot infection may be faster with this approach, although the data supporting topical antibiotics is weak and based on poorly designed trials.31 Surgical treatment plays a significant role in the management of diabetes-related foot infection. Tissue and bone cultures obtained during surgical interventions help guide antibiotic selection. Many patients need sharp surgical debridement by a wound care clinician or surgeon to remove necrotic tissue or calluses and aid in the formation of granulation tissue capable of re-epithelialization.6 Shared decision-making with patients is important because surgical procedures range from bedside debridement to major amputation. Amputations are devastating psychologically, and many patients fear amputation more than death.32 Surgical intervention is needed for gangrene, necrotizing fasciitis, or significant abscess formation. Although surgical resection of osteomyelitis was traditionally the standard of care, emerging evidence suggests most infections respond well to antibiotic therapy alone.6 In patients with a diabetes-related foot infection and ischemia, vascular interventions should be considered to improve a patient's treatment response and lower the risk of recurrence.17 The Wound, Ischemia, foot Infection score predicts clinical outcomes and guides interventions in patients with more advanced disease.33,34 The Wound, Ischemia, foot Infection scoring system factors in the International Working Group on the Diabetic Foot infection grade, objective measures to determine the extent of ischemia, and the anticipated likelihood of wound healing. These factors combine to stage wounds from 0 to 3 with higher scores requiring more invasive surgical management, including amputation.18 Wound therapy in a patient with a diabetes-related foot infection is complex and often requires team-based care. Comprehensive wound care may include debridement, application of moist dressings, and the use of off-loading orthotics to reduce pressure on a wound.6 A moist dressing is preferred to aid in healing and help with infection control. It is unknown if any specific dressing is more effective because of a lack of head-to-head trials.35 Redistribution of pressure off the plantar surface is important because this is the main cause of foot ulcers and, if not addressed, may inhibit ulcer healing. Strategies to help with off-loading pressure include changes to a patient's shoes, specialized boots, or orthotic walkers.36 Studies of adjunctive treatments (e.g., hyperbaric oxygen therapy, maggot debridement therapy, granulocyte colony-stimulating factors, topical oxygen therapy, laser therapy) for healing diabetes-related foot ulcers have mixed results. Of these alternative treatments, hyperbaric oxygen therapy has the best data, with evidence showing that it lowers the risk of major amputations and improves wound healing; however, evidence does not support reductions in minor amputations or mortality.37 Maggot debridement therapy has good data, with evidence for shortening ulcer healing time and reducing the rate of amputations.38 Granulocyte colony-stimulating factors have not been shown to help resolve an infection or foot ulcer significantly, but they may decrease the risk of surgical interventions and amputations.39 Promising evidence exists for topical oxygen therapy and laser therapy for improving diabetes-related foot ulcer healing; however, more evidence is needed on patient-oriented outcomes before widespread adoption of either intervention.40,41 Little evidence exists for primary prevention strategies of diabetes-related foot ulcers or infections despite widespread support for these interventions.42 Guidelines strongly support systematic assessment, foot care counseling, and comorbidity management for primary prevention because these strategies are useful in secondary prevention, and complications from a diabetes-related foot infection are significant.6,43 Recognition of a patient with neuropathy is critical considering the high rate of patients who are asymptomatic. Conducting a foot examination may take only three minutes and can be organized into three parts (patient history, physical examination, patient education).5 Team-based care for primary prevention may include nurses, pharmacists, podiatrists, and other clinicians. Secondary prevention of diabetes-related foot ulcers and infections starts with frequent, systematic assessments recommended by guidelines such as the American Diabetes Association's Standards of Medical Care. These guidelines highlight the importance of a comprehensive foot examination at least annually, and for every diabetes care visit for individuals at high risk of an infection (e.g., poor circulation, history of amputation, severe neuropathy).43 All patients with diabetes should receive counseling on foot care and how to choose appropriate footwear. Using therapeutic footwear is often unnecessary; however, it should be considered in high-risk patients (e.g., severe neuropathy, foot deformities, ulcers, poor circulation, history of amputation).43 Other preventive techniques include improving glucose control, smoking cessation, daily foot inspection, debridement of calluses, and monthly physician foot checks for patients with end-stage renal disease requiring dialysis.42–45 Interventions to prevent an ulcer or diabetes-related foot infections are summarized in Table 3.5,42–45 Data Sources: A PubMed search was completed in Clinical Queries using the key terms diabetic foot ulcers, infections, antibiotics, statistics, pharmacological, and prevention. The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. Also searched were Access Medicine, the Cochrane Library, Lexicomp, the National Guideline Clearinghouse database, and UpToDate. Search dates: October 27, 2020 to November 4, 2020, and April 26, 2021. Figure 1 and Figure 2 provided courtesy of Joshua Visserman, MD. Page 10 Osteomyelitis is an inflammatory condition of bone secondary to infection; it may be acute or chronic. Symptoms of acute osteomyelitis include pain, fever, and edema of the affected site, and patients typically present without bone necrosis in days to weeks following initial infection. Chronic osteomyelitis develops after months to years of persistent infection and may be characterized by the presence of necrotic bone and fistulous tracts from skin to bone.1,2 Osteomyelitis is further classified by mechanism of infection as hematogenous or nonhematogenous. With hematogenous osteomyelitis, bacteria are seeded into bone secondary to a bloodstream infection and the condition is most common in children, older adults, and immunocompromised populations.1–3 Nonhematogenous osteomyelitis occurs from direct inoculation in the setting of surgery or trauma or with spread from contiguous soft tissue and joint infections.1,2 Methicillin-sensitive Staphylococcus aureus is the most frequently identified pathogen across all types of osteomyelitis, followed by Pseudomonas aeruginosa and methicillin-resistant S. aureus. Hematogenous osteomyelitis is often monomicrobial and can occur from aerobic gram-negative rods or from P. aeruginosa or Serratia marcescens in injection drug users.4 Vertebral osteomyelitis is the most common type of hematogenous osteomyelitis and is polymicrobial in 5% to 10% of cases.1 Blood cultures may be negative if osteomyelitis develops following bacterial clearance from the bloodstream. Nonhematogenous osteomyelitis can be polymicrobial; S. aureus is the most common pathogen in addition to coagulase-negative staphylococci and gram-negative aerobes and anaerobes. Polymicrobial diabetic foot infections and decubitus ulcers may include Streptococcus species and Enterococcus species.1 Less common pathogens can be associated with certain clinical conditions, including immunocompromise (Aspergillus species, Mycobacterium tuberculosis, Candida species), sickle cell disease (Salmonella species), HIV infection (Bartonella henselae), and tuberculosis (M. tuberculosis).1,5,6 The clinical presentation of nonhematogenous osteomyelitis varies and symptoms are often non-specific. Signs and symptoms common to all sub-types may include pain, edema, and erythema. Acute osteomyelitis may present with a more rapid onset of symptoms (development over days) and is more likely to be associated with fever. Systemic symptoms are not common in chronic osteomyelitis, and the presence of fistulous tracts from skin to bone is diagnostic. Long-standing, nonhealing ulcers and nonhealing fractures may also be associated with chronic osteomyelitis. Patients with diabetic neuropathy are at higher risk of developing osteomyelitis secondary to local spread from diabetic foot infections and unrecognized wounds.2 Smoking increases the risk of osteomyelitis from diabetic foot infections and healing fractures.7 Peripheral vascular disease and poorly healing wounds (e.g., decubitus ulcers) are more likely to lead to bone inflammation. Osteomyelitis secondary to diabetic foot ulcers can be difficult to diagnose given chronic changes from vascular insufficiency and ischemia.8 Hematogenous osteomyelitis often presents similarly to nonhematogenous disease. The most common form of hematogenous osteomyelitis is vertebral; patients often have back or neck pain and muscle tenderness, sometimes followed by fever. Hematogenous osteomyelitis may also occur in the sternoclavicular, pelvic, and long bones.9 When hematogenous osteomyelitis affects prepubertal children, it typically occurs in the metaphysis of long bones adjacent to growth plates, with a predilection for the tibia and femur.1 A diagnosis of osteomyelitis should be considered in any patient with acute onset or progressive worsening of musculoskeletal pain accompanied by constitutional symptoms such as fever, malaise, lethargy, and irritability. Constitutional symptoms do not always occur in adults, especially in the setting of immunocompromise. The index of suspicion for osteomyelitis should be higher in patients with underlying conditions, including poorly controlled diabetes mellitus, neuropathy, peripheral vascular disease, chronic or ulcerated wounds, history of recent trauma, sickle cell disease, history of implanted orthopedic hardware, or a history or suspicion of intravenous drug use. A dedicated physical examination can increase the likelihood of diagnosing osteomyelitis if findings include erythema, soft tissue infection, bony tenderness, joint effusion, decreased range of motion, or exposed bone. The probe-to-bone test may be useful to rule out diabetic foot osteomyelitis in low-risk patients.10,11 The differential diagnosis of osteomyelitis includes soft tissue infection, gout, Charcot arthropathy, fracture, malignancy, bursitis, osteonecrosis, sickle cell vasoocclusive pain crisis, and SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis). Uncertain clinical diagnosis should prompt further workup that includes laboratory evaluation and imaging (Table 12,9,12,13). Definitive diagnosis is made with a positive culture from biopsy of the affected bony structure. Polymerase chain reaction testing may help in the rapid diagnosis of organisms or for cultures taken after antibiotic therapy.12,14 Bone biopsy remains the diagnostic standard but is not always feasible. Some evidence suggests that biopsy should be reserved only for select cases because the results may not lead to treatment alterations.15 Initial laboratory evaluation should include a complete blood count, erythrocyte sedimentation rate, C-reactive protein, and blood cultures. Leukocytosis may be present in acute osteomyelitis, but it can be absent in chronic osteomyelitis.16,17 There is some evidence that thrombocytosis may positively predict osteomyelitis in patients with chronic leg ulcers.18 If inflammatory markers are elevated, they can be trended for clinical correlation.19,20 Positive blood cultures in association with radiographic evidence of osteomyelitis may prevent the need for a more invasive bone biopsy.21 Plain film radiography is the first-line evaluation of suspected osteomyelitis. Advanced imaging is often needed for diagnosis following plain film radiography, because 50% to 75% of the bone matrix must be destroyed before lytic changes are evident on plain radiographs.22 Findings can include soft tissue swelling, osteopenia, cortical loss, bony destruction, and periosteal reaction12,23,24 (Figure 12). Advanced imaging can be guided by onset of symptoms and patient variables (Table 22,9,13,24–30). Magnetic resonance imaging (MRI) has a high sensitivity and negative predictive value. Plain radiography and MRI are often both indicated and complementary13 (Figure 2, Figure 3, and Figure 4). Although contrast media is not required for diagnosis, it may be helpful to distinguish between abscess and phlegmon, especially in patients with chronic osteomyelitis.25–27 MRI is more readily available and avoids radiation exposure, but positron emission tomography (PET) and single-photon emission computed tomography (SPECT) can also reliably diagnose osteomyelitis.25 In patients in whom MRI is contraindicated, a tagged leukocyte scan, computed tomography (CT), PET/CT, or sulfur colloid marrow scan can be appropriate; however, diagnosis may be impeded because of false-positive results from recent surgery or trauma, healed osteomyelitis, arthritis, bony tumors, Paget disease of bone, or reduced uptake secondary to necrosis and poor blood flow.13,29,30 Ultrasonography plays a complementary role to other modalities and may demonstrate inflammatory changes in the periosteum, particularly in children. Ultrasonography can be useful for identification of soft tissue abscess and helpful for abscess aspiration.13 Osteomyelitis treatment requires a multifaceted approach that may include antibiotics, surgical intervention, and other modalities depending on multiple clinical factors, including clinical stage. Clinical staging guides decision-making when choosing specific surgical treatments and limits the need for amputation.31 The 2015 modification of the Cierny-Mader staging system (developed in 1985) is commonly used and classifies osteomyelitis based on the anatomic location and the physiologic condition of the patient.31,32 Anatomic types include medullary (stage 1), superficial (stage 2), localized (stage 3), and diffuse (stage 4), with higher stages requiring more complex surgical intervention.32 The physiologic condition of the patient (host) can be classified as type A (normal immune response and healthy vascular system), type B (local immunocompromise), or type C (noncandidate for surgery). In those classified as type C, treatment is expected to cause more harm than the disease process itself, so the focus of care shifts from cure to palliation. The choice of antibiotic therapy is specific to the culture results listed in Table 3.2,33–37 It should be tailored to the individual patient based on susceptibility. Specific antibiotic coverage is usually indicated. In hospitalized patients at risk of methicillin-resistant S. aureus, empiric antibiotic coverage is recommended. Delaying antibiotic therapy until cultures are available is recommended except in patients in whom urgent intervention is necessary, such as those with severe sepsis, epidural extension, or neurologic involvement. The addition of rifampin to other antibiotics may also improve cure rates, especially when prosthetic joint or spinal implant infections are present.35,36 For adult patients hospitalized with osteomyelitis, parenteral followed by oral antibiotic therapy appears to be as effective as long-term parenteral therapy. Evidence suggests that oral antibiotics have similar cure rates and lower risks and costs compared with parenteral antibiotics.20,37,38 Treatment typically lasts four to six weeks, but comparisons of treatment duration have not been well studied.37 Surgical bony debridement followed by drainage of any associated soft tissue abscess continues to be a mainstay of therapy, although there is no clear recommendation about which cases will require debridement.36 Debridement is typically indicated as part of the initial treatment in the presence of underlying orthopedic hardware and necrotic bone. Stabilization of the bone is an essential component of debridement and can decrease healing time and complications. Surgical debridement after antibiotic therapy shortens hospital stays, reduces medical costs, provides satisfactory infection control, and prevents complications of long-term systemic antibiotic use.39 Debridement can be supplemented with the placement of antibiotic-loaded collagen sponges, which has some evidence supporting improved outcomes.40 Hyperbaric oxygen therapy can be used as an adjunctive modality and may be particularly helpful in cases of chronic osteomyelitis.41 When selecting treatment strategies for osteomyelitis, several groups of patients require special considerations, such as children and patients who have prosthetic joints, vertebral osteomyelitis, and diabetes. The treatment of these groups is beyond the scope of this article. Data Sources: A PubMed search was completed in Clinical Queries using the key terms osteomyelitis, imaging, diagnosis, and treatment. The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. Also searched were the Cochrane database, the Database of Abstracts of Reviews of Effectiveness (DARE), Dynamed, and Essential Evidence Plus. Search dates: August 11, 2020, and March 10, 2021. Figure 2, Figure 3, and Figure 4 provided by Timothy G. Russell, MD, Department of Radiology, Martin Army Community Hospital. The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army at large. Page 11 Air travel has become increasingly popular over time, despite decreases during the COVID-19 pandemic, with 1.1 billion total passengers in 2019 and most Americans having flown at least once in the past three years.1 Air travel is generally safe, but especially for the aging U.S. population, the flight environment poses unique physiologic challenges, particularly relative hypoxia, which may trigger adverse myocardial or pulmonary outcomes. To optimize health outcomes, communication must take place between the traveler, family physician, and airline carrier when any doubt occurs about fitness for air travel. Travelers should carry current medications in their original containers as well as a list of their medical conditions and allergies and should adjust timing of medications as needed based on time zone changes. Travelers should also consider available medical resources at their travel destinations and layover locations. Family physicians and travelers can review relevant pretravel health information, including required and recommended immunizations, health concerns, and other travel resources appropriate for any destination worldwide at . By law, U.S. commercial aircraft cannot exceed a relative cabin altitude of 8,000 feet (2,438 m) because of the potential for significant hypoxia above this altitude.2 Most passengers exposed to this environment will have a partial pressure of arterial oxygen (Pao2) of 60 to 65 mm Hg (7.98 to 8.64 kPa), corresponding to 89% to 94% peripheral oxygen saturation (Spo2), which may compromise cardiovascular or pulmonary disease in affected travelers.3 Neither reassuring pulse oximetry nor reassuring forced expiratory volume in one second has been found to predict hypoxemia or in-flight events for patients with pulmonary conditions.3 The nonstandardized Hypoxia Altitude Simulation Test, administered and interpreted by pulmonologists, can be used to determine specific in-flight oxygen requirements for patients with pulmonary complications or those for whom safe air travel remains in doubt. Typically, the Hypoxia Altitude Simulation Test comprises breathing 15% fraction of inspired oxygen for 20 minutes, with pulse oximeter and blood gas measurements taken before and after testing.4–6 Patients with a Hypoxia Altitude Simulation Test Pao2 less than 50 mm Hg (6.65 kPa) at any point during the test require supplemental oxygen in flight, whereas those with a Pao2 greater than 55 mm Hg (7.32 kPa) do not. Pao2 measurements falling between 50 and 55 mm Hg are considered borderline and may necessitate further testing with activity.5 Given that the test itself incurs some risk and may not be available to all travelers, family physicians can counsel patients who are unable to walk 50 m (164 ft) or those whose usual oxygen requirements exceed 4 L per minute not to fly.3,4,7,8 Patients with oxygen requirements less than 4 L per minute can be counseled to double their usual flow rate while flying.8 Commercial airline carriers usually permit the use of personal Federal Aviation Administration–approved portable oxygen compressors, but carriers require travelers to give from 48 hours to one month's notice before flight when they are requesting the use of compressed oxygen.9 Table 1 lists indications for which further assessment (e.g., Hypoxia Altitude Simulation Test, ability to walk 50 m) is warranted, including previous respiratory difficulties while flying, severe lung disease, recent or active lung infections, any preexisting oxygen requirements or ventilatory support, or if less than six weeks have passed since hospital discharge for acute respiratory illness.3 Patients who have undergone an open-chest lung procedure should defer travel for two to three weeks, must not have any recent or residual pneumothorax, and should be assessed for supplemental oxygen needs.10 Travelers with underlying cardiac conditions should use airport assistance services such as wheelchairs and baggage trolleys to decrease myocardial oxygen demand.9 Although most cardiac conditions are safe for flight, some require additional consideration. Travelers with minimally symptomatic, stable heart failure may safely fly, but medication adherence is critical.9,11 Patients with stable angina should be assessed for oxygen needs if they become short of breath after walking 50 m, and they should not fly following any recent medication changes that have not demonstrated clinical stability beyond that medication's half-life.7,11 Patients with unstable angina, new cardiac or pulmonary symptoms, or recent changes in medication without appropriate follow-up should not fly until stable, particularly for medication changes that could impact blood pressure or coronary reserve.11 Travelers with recent myocardial infarction at low risk should defer air travel for three to 10 days postevent11–15 (Table 211). Low-risk patients who required percutaneous transluminal coronary angioplasty may fly after three days as long as they are asymptomatic.9 Travelers who have had coronary artery bypass grafting or an uncomplicated open-chest procedure should wait to fly until they are 10 days postprocedure.7,11 Many implantable-cardioverter defibrillators are compatible with standard airport security.9 The Transportation Security Administration recommends that travelers with pacemakers, defibrillators, or any other implanted metal device request pat-down screening instead of using a walk-through metal detector.16 For travelers with pacemakers and implantable-cardioverter defibrillators, a two-day flight restriction following uncomplicated placement is appropriate.11 It is prudent for all cardiac patients to travel with a copy of their most recent electrocardiography results and a preflight graded exercise test, which may aid in assessment and management in case of an event during flight.9 In patients with hypertension, medication compliance is especially important because aircraft noise and other travel-related stress may provoke blood pressure elevations.17 Travel in patients with moderately controlled hypertension is not a contraindication, but airline travel for those with uncontrolled hypertension requires shared decision-making and clinical judgment. Ear, Nose, and Throat Conditions Trapped gases and sinus air-fluid levels can cause significant pain for the patient with ear, nose, and/or throat conditions. Adult patients with symptomatic rhinosinusitis or allergic rhinitis may benefit from oxymetazoline (Afrin) and/or pseudoephedrine to prevent ear blockage during descent.18 No evidence suggests that antihistamines or decongestants are beneficial in children with sinusitis,19 and these medications should not be used to hasten an early clearance for flight in any age group. Flight within 36 hours of otitis media resolution is generally safe.20 Equalizing pressure on descent can also be accomplished in adults with frequent swallowing, chewing gum or food, or by generating pressure against a closed mouth and glottis. In young children and infants, upright bottle feeding or pacifier use can achieve similar effects.21 Patients who have undergone jaw fracture repair should defer flying for at least one to two weeks, and jaw wiring should be temporarily replaced with elastic bands in case of emesis.18 Transdermal scopolamine is effective in preventing air sickness,22 and alternatives such as first-generation antihistamines may also be useful. Patients who elect to take scopolamine should be counseled on adverse effects of drowsiness, blurry vision, dry mouth, or dizziness.22 Individuals who are prone to air sickness should refrain from alcohol use during flight and in preflight and should eat smaller, lighter meals.18 The expansion of trapped gas at altitude may cause severe tooth pain in patients with caries beneath fixed restorations. Travelers with hearing aids should bring extra batteries and all accessories and may need to adjust their volume levels to offset background noise. In addition to carrying all medications, travelers with diabetes requiring insulin should request appropriate meals and consider checking blood glucose levels at intervals during longer flights.23 Bringing snacks or other food can assist those with tenuous diabetes management in the event of layovers or delays. Insulin requirements may change based on the direction of travel and crossing time zones, which may entail lost or gained hours. Even if it is not part of the patient's normal regimen, fast-acting insulin, ideally with a pen device, should be considered for all travelers during flight due to its flexibility and responsiveness.23 When traveling east, if the day is shortened by two or more hours, it may be necessary to give less insulin on the first day at the destination. When traveling west, if the day is extended by two or more hours, it may be necessary to give more insulin on the first day at the destination. Blood glucose should be checked at least 10 hours after the first-day dose to allow for further adjustments. Travelers can return to their normal insulin regimen on day 2 at their destination. A comprehensive public access resource for medical

professionals addressing insulin adjustment for the air traveler is available through the Aerospace Medical Association.23 Gastrointestinal Conditions For travelers with recent intra-abdominal procedures, trapped gas expansion could disrupt sutures and cause rebleeding. Travelers should wait until 24 hours have passed and any bloating has resolved following laparoscopic abdominal procedures or colonoscopy.7,10 Travelers should wait one to two weeks after open abdominal surgery.10 Patients with active gastrointestinal problems, including hematemesis, melena, or obstruction, should not fly.24 A baseline anemia may predispose travelers to syncope given the relative hypoxia of the flight environment. Caution should be exercised for travelers with a hemoglobin level below 8.5 g per dL (85 g per L), and some authorities recommend not advising flight for any travelers with levels below 7.5 g per dL (75 g per L).7 Young, otherwise healthy patients with chronic anemia may be more tolerant of relative hypoxia, especially if their hemoglobin level is greater than 7.5 g per dL.24 For the traveler with sickle cell anemia, sickling crisis during flight is unlikely24; however, flight should be delayed for 10 days following an acute crisis, and patients with sickle cell anemia who have received a recent transfusion should not fly if hemoglobin levels are less than 7.5 g per dL.24 Although deep venous thrombosis (DVT) is not caused by the flight environment itself, DVT is a concern for people who sit for extended periods or have risk factors.25 Incidence of DVT reaches up to 5.4% in high-risk groups flying an average of 12.4 hours.26 Compression stockings can prevent asymptomatic DVT and superficial venous thrombosis in flights lasting five hours or longer.27 Table 3 lists recommendations for DVT prophylaxis for travelers who are at low, moderate, and high risk for DVT.11 The baseline recommendations for each group include staying hydrated, avoiding alcohol to prevent dehydration, walking at least 10 to 15 minutes in each two hours of travel time, and performing isometric exercises while seated.11 When indicated for high-risk travelers, including those with reduced mobility, low-molecular-weight heparin (e.g., 40 mg of subcutaneous enoxaparin [Lovenox]) on the day of and day after travel is appropriate for anticoagulation.28 Psychiatric and Intellectual Disability Conditions Passengers with mental or intellectual disabilities often benefit from a traveling companion because physiologic stresses of flight and the chaotic nature of busy airports may be especially challenging aspects of travel for these groups.9 Prescription anxiolytics may alleviate travel anxiety, but a test dose is highly encouraged before flight.9 Service or emotional support animals can be used for a variety of mental health conditions; an article in American Family Physician provides information about considerations for documentation for emotional support animals.29 See the U.S. Department of Transportation website for current guidelines regarding the use of these animals during air travel.30 Passengers predisposed to stress-related headaches and severe migraines should always carry abortive medications. Travelers with uncontrolled vertigo are not good candidates for flight. Patients prone to syncope should remain well-hydrated and be cautioned to avoid alcohol or quickly standing from a seated position. One small study suggests that people who have epilepsy with a history of flight-related seizures and a high baseline seizure frequency are likely to have a seizure after flying.31 The Aerospace Medical Association recommends that patients with uncontrolled or poorly controlled seizures should not fly.32 A safe amount of time permitted before flight following a seizure has not been established, but clinical judgment and the presence of a knowledgeable chaperone should factor into any medical recommendation. Although some airline carriers allow patients to fly 72 hours after a stroke,7 the Aerospace Medical Association recommends waiting one to two weeks.32 Background radiation associated with the flight environment does not pose a special hazard for most pregnant air travelers; however, the Federal Aviation Administration recommends informing aircrew or frequent flyers about health risks of radiation exposure.33 Because a lack of in-flight medical resources may jeopardize safety of the mother and neonate, patients with an uncomplicated singleton pregnancy should generally not fly beyond 36 weeks of estimated gestational age7,24,33,34 and those with a multiple gestation not beyond 32 weeks.7,34 Body imaging scanners are safe for security screening during pregnancy.34,35 Postpartum travelers are at moderate risk for DVT and should wear compression stockings and perform isometric exercises during flight.11 Travelers who have undergone an uncomplicated cesarean delivery are generally safe for flight within one to two weeks.10 Ophthalmologic Conditions Passengers with severe visual impairment may benefit from having a traveling companion. Xerophthalmia may be exacerbated in the low humidity of the airplane cabin, and lubricating eye drops are advisable. Cataracts and clinically stable glaucoma are not contraindications to flight; however, any retinal detachment interventions should restrict flight for at least two weeks.36 Open-globe eye surgery should delay air travel for up to six weeks, and travel recommendations should be made in conjunction with an ophthalmologist.36 Because of expansion of trapped air at altitude, all fixed casts should be bivalved.7,37 Some airlines do not permit air casts of any kind, but if they are used, a small amount of air should be released to prevent any limb compression that occurs as a result of trapped gas expansion. Elastic bandages can be added to a bivalved cast and can be loosened as tolerated. The Transportation Security Administration recommends that passengers with prosthetic limbs should avoid metal detector screening and should be screened with alternative measures.16 Individuals with significantly decreased mobility should consider wheelchairs and the use of travel companions. Passengers with low back pain and other mobility-limiting conditions can request seating near the front to reduce walking; however, business and first-class seating is an additional cost. Foley catheters and other inflatable balloons are compatible with flight; however, they should be filled with liquid for air travel, given the previously described expansion of trapped gas at altitude. Special Considerations for Children Healthy, term neonates should not fly for at least 48 hours after birth but preferably one to two weeks.21 Infants younger than one year with a history of chronic respiratory problems since birth should be evaluated by a pulmonologist before air travel.3 Other Air Travel Considerations Jet lag occurs as a result of desynchronization between an individual's internal circadian rhythm and the external environment's time zone.38,39 Jet lag is worse for eastward rather than westward travel.40 Measures for prevention include ensuring enough sleep before travel, timing light exposure using sunglasses, avoiding alcohol, and eating at appropriate times after arriving at the destination. Timed melatonin is highly effective at treating jet lag,41 and prescription hypnotic-sedative medications may also work in controlling sleep loss.38 Self-contained underwater breathing apparatus (SCUBA) divers should not fly within 12 hours of a dive because of the concern for decompression sickness or life-threatening arterial gas embolism.42 The airplane cabin does not inherently pose greater risk for infection than any other close contact, but respiratory viral pathogens are the most commonly transmitted infections.43 Because of the ongoing COVID-19 pandemic, the Centers for Disease Control and Prevention (CDC) recommends delaying travel until the individual is fully vaccinated because traveling increases the chance of getting and spreading COVID-19. For patients not fully vaccinated who must travel, it is important to follow the CDC's recommendations for unvaccinated people. Check for evolving guidelines on the CDC's website.44 Patients with breast cancer who have had surgery may fly without risking new or worsening lymphadenopathy.45 A comprehensive discussion of in-flight emergencies is beyond the scope of this article. See the American Family Physician article on in-flight emergencies for more details.46 Data Sources: A PubMed, Cochrane database, Essential Evidence Plus, ACCESSSS, and ECRI search occurred in April and May 2020 and April and May 2021 using search terms aviation medicine, travel medicine, commercial flight, air travel, and fitness to fly. The Aerospace Medical Association's website resource, Medical Considerations for Airline Travel, was searched in its entirety. The Handbook of Aviation and Space Medicine, Fundamentals of Aerospace Medicine, and Aviation and Space Medicine were reviewed for clinically relevant chapters. The authors acknowledge Rachel Kinsler, USAARL Research Engineer, for her thoughtful review of this manuscript. The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation. Citation of trade names in this report does not constitute an official Department of the Army endorsement or approval of the use of such commercial items. Page 12 A 36-year-old patient, L.B., with a history of hypertension presents for a wellness visit. The patient's mother had a stroke at 65 years of age and the patient's older brother recently had a heart attack. L.B. has an estimated 10-year cardiovascular risk of 6%, and L.B.'s body mass index is 29 kg per m2. The rest of the patient's history and physical examination is unremarkable. 1. According to the U.S. Preventive Services Task Force (USPSTF), which one of the following is the most appropriate behavioral counseling approach to promote a healthy diet and physical activity to prevent cardiovascular disease? A. Providing educational materials on healthy eating and ways to improve physical activity level.B. No counseling should be provided because there is little to no net benefit of counseling for this patient.C. Providing a one-time, in-office counseling visit on healthy eating and physical activity, with motivational interviewing techniques and goal setting.D. Providing intensive behavioral counseling on healthy eating and physical activity, with multiple contacts over an extended period. 2. The USPSTF recommends offering behavioral counseling for cardiovascular disease prevention to patients with which one of the following cardiovascular risk factors? A. Abnormal blood glucose level.B. Obesity.C. Smoking.D. Estimated 10-year cardiovascular risk of 7.5% or greater. 3. According to the USPSTF, which of the following statements about benefits and harms of behavioral counseling to promote a healthy diet and physical activity are correct? A. There is inadequate evidence that counseling interventions improve blood pressure.B. There is adequate evidence that counseling interventions improve healthy eating habits.C. There is adequate evidence that counseling interventions reduce overall cardiovascular disease events.D. There is inadequate evidence to determine the harms of counseling interventions. The correct answer is D. The USPSTF recommends offering adults with cardiovascular risk factors behavioral counseling interventions to promote a healthy diet and physical activity.1 Interventions that have been shown to reduce cardiovascular risk include a combination of counseling on healthy diet and physical activity that incorporates behavioral change techniques and can include individual or group counseling sessions. Interventions typically include multiple contacts over an extended period (with a median of 12 contacts and six hours of contact over 12 months).2 The correct answer is D. The USPSTF recommends offering behavioral counseling interventions to adults at increased risk of cardiovascular disease, defined as those with hypertension, dyslipidemia, or multiple risk factors such as metabolic syndrome or an estimated 10-year cardiovascular disease risk of 7.5% or greater. This recommendation does not apply to adults with other cardiovascular risk factors such as diabetes mellitus, abnormal blood glucose levels, obesity, or smoking. Guidance on reducing cardiovascular disease risk in these populations (as well as individuals with other modifiable risk factors) are addressed in separate USPSTF recommendations.The correct answers are B, C, and D. The USPSTF found adequate evidence that counseling interventions reduce overall cardiovascular disease events and improve healthy eating habits. It found convincing evidence that counseling interventions improve blood pressure, lipid and fasting blood glucose levels, and body weight. The USPSTF found inadequate evidence to determine the harms of counseling interventions, although based on the nature of the interventions (counseling or physical activity), the harms are thought to be no greater than small in magnitude. The views expressed in this work are those of the authors and do not reflect the official policy or position of Johns Hopkins Bloomberg School of Public Health or the U.S. government. This series is coordinated by Kenny Lin, MD, MPH, deputy editor. Page 13 A 17-year-old patient presented with a lump on the head. The patient first noticed the lump at 11 years old. It had been slowly growing over the previous few years. The lump was not painful and did not bleed. It occasionally itched and bothered the patient when they brushed their hair. The patient did not recall injury or trauma to the area. Physical examination revealed a skin-colored polypoid mass on the top of the patient's head, above the parietal area (Figure 1). The mass was raised and asymmetrical with slightly irregular borders. It measured 14 mm × 12 mm in size. Based on the patient's history and physical examination findings, which one of the following is the most likely diagnosis? A. Acrochordon.B. Compound nevus.C. Dermal nevus.D. Junctional nevus. The answer is C: dermal nevus. Commonly called moles, nevi are benign tumors composed of nevus cells. They can be acquired or congenital. Nevi appear on 1% to 2% of newborns and increase in incidence throughout life, peaking in the 30s and 40s. Most nevi are benign. However, some, such as large congenital nevi and atypical moles, may become malignant. Congenital nevi are considered large in adults if they are at least 20 cm in diameter and in neonates if they are at least 9 cm on the head or neck or 6 cm on other areas.1–4 The three subtypes of nevi (compound, dermal, and junctional) are differentiated by the location of the nevus cells in the skin. Nevus cells typically start in the dermoepidermal junction and migrate into the dermis. During the transition, a lesion is considered a compound nevus. The development is sequential, and progression can stop at any point.3,5 The shape and size of dermal nevi vary widely. They can be warty, polypoid, or pedunculated. Like the other subtypes, dermal nevi can be hyperpigmented or pink or appear the same color as surrounding skin.1,5 Acrochordons are commonly known as skin tags. They are usually the color of surrounding skin but can be hyperpigmented. They are often pedunculated and range from 2 mm to 5 mm in size but can be larger. They increase in number with age and during pregnancy.6 Compound nevi are usually hyperpigmented or the color of surrounding skin with a smooth and elevated or warty surface. Elevation may increase with age. They are usually round or oval and symmetrical. Hair may be present.1,5 Junctional nevi are usually hyperpigmented and typically flat, but they can be slightly raised. They are usually round or oval with symmetrical borders. Progression to melanoma is rare; however, they may change into compound nevi with cells from the dermis and the junctional area. Most junctional nevi are hairless.1,5 Page 14 A 71-year-old patient presented to the family medicine office for routine preventive care. The patient reported having a rash that developed one month earlier. The rash appeared spontaneously and was not associated with systemic symptoms, such as fevers or chills. The patient did not have photosensitivity. The patient had no relevant contact exposures, including new personal hygiene or cleaning products, and was not taking any new medications. The patient did not have a history of dermatologic disease, diabetes mellitus, or known malignancy. Physical examination revealed a pruritic, nonscaly, ring-like rash, mostly localized on the dorsa of both hands (Figure 1). Based on clinical appearance, the patient was empirically treated for a dermatophyte infection, but the rash persisted and spread to the forearms (Figure 2). A punch biopsy of the lesion on the hand was performed. Based on the patient's history and physical examination findings, which one of the following is the most likely diagnosis? A. Erythema annulare centrifugum.B. Granuloma annulare.C. Subacute cutaneous lupus erythematosus.D. Tinea corporis. The answer is B: granuloma annulare, a benign, idiopathic, granulomatous skin disease that is more common in women. Granuloma annulare can be localized or generalized. Localized granuloma annulare occurs most often on the dorsal or lateral surfaces of the hands or feet. The lesions present as nonscaly, skin-colored or erythematous, annular plaques with a firm, rope-like border and central clearing. Generalized granuloma annulare presents as multiple widespread, skin-colored to erythematous papules and plaques that vary in size and predominately occur on the trunk and extremities. Granuloma annulare can be distinguished from other annular skin conditions by the lack of scaling or other surface changes to the skin. The localized type is more common in younger adults, whereas generalized granuloma annulare has a bimodal distribution.1–3 Localized granuloma annulare is likely to resolve spontaneously within months or a few years, but the generalized form is more chronic and less responsive to treatment. The literature on treatment is limited to case reports and small uncontrolled studies. Typical treatments include topical therapies, systemic immunosuppressive therapies, and phototherapy. High-dose systemic steroids have been shown to be beneficial; however, symptoms often recur after discontinuation of treatment. The exact cause of the condition is unclear, but potential associations have been reported between both types of granuloma annulare and diabetes mellitus, thyroid disease, hyperlipidemia, malignancy, insect bites, and viral disease.1–3 Erythema annulare centrifugum is a delayed-type hypersensitivity reaction manifesting as annular, erythematous plaques with a trailing rim of scale. A paraneoplastic erythema annulare centrifugum eruption may also occur, with an erythematous lesion and urticarial type papules that enlarge centrifugally and then clear centrally.4 Subacute cutaneous lupus erythematosus is often associated with systemic lupus erythematosus. Lesions present as small, erythematous, scaly macules or papules that develop into psoriasiform or annular/polycyclic plaques. The predominant distribution is on sun-exposed areas such as the upper back, shoulders, neck, and anterior chest, and the rash is highly photosensitive. Up to one-third of cases are drug-induced. Causative medications include antihypertensives, anticonvulsants, proton pump inhibitors, and tumor necrosis factor–alpha inhibitors.5,6 Tinea corporis (ringworm) is a common, cutaneous dermatophyte infection that presents as a pruritic, well-demarcated, sharply circumscribed, erythematous, scaly patch with central clearing, leaving an actively advancing raised border. Most cases of tinea corporis respond to topical antifungals, although systemic therapy may be required with extensive skin involvement.7 Page 15 Does light therapy decrease depression in older adults without seasonal depression? Light therapy appears to be mildly effective in treating depression in older adults, but ideal wavelength, intensity, and length of treatment are unknown. (Strength of Recommendation [SOR]: B, based on a systematic review of randomized controlled trials [RCTs] with heterogeneity and extrapolated from systematic reviews of RCTs of adults of all ages.) In adults, bright white light exposure in the mornings for less than 60 minutes may be most effective. (SOR: B, based on a systematic review of RCTs.) A 2018 systematic review and meta-analysis of six RCTs (N = 359) examined the effectiveness of light therapy among patients older than 60 years with nonseasonal depression.1 The trials compared light therapy (of varying wavelength, intensity, and duration) to either dim red or white light, nothing, or usual therapy. Trials were conducted for four weeks (three trials), three weeks (one trial), or no more than two weeks (two trials). The pooled results of all trials found that geriatric depression symptoms improved more with a small to moderate effect in the light therapy groups compared with the control groups (standardized mean difference [SMD] = 0.45; 95% CI, 0.14 to 0.75). Subgroup analysis by length of intervention revealed no statistically significant differences between treatment and control groups at two weeks (two trials; n = 117; SMD = −0.18; 95% CI, −0.54 to 0.18; I2 = 0%), three weeks (two trials; n = 165; SMD = 0.38; 95% CI, −0.36 to 1.13; I2 = 83%), or four weeks (three trials; n = 179; SMD = 0.25; 95% CI, −0.05 to 0.54; I2 = 0%). In all six trials, there were no significant adverse reactions in the treatment group. The treatment and control groups did not differ in the rates of adverse reactions reported. Because of limited available evidence, the authors were not able to make conclusions regarding the ideal wavelength, intensity, or duration of light therapy in the study population. The findings are limited by moderate heterogeneity (I2 = 50%). A 2020 systematic review and meta-analysis of 23 RCTs (N = 1,120) examined the effectiveness of light therapy in adults of all ages with nonseasonal depression.2 The studies compared light therapy (of varying wavelength, intensity, and duration) with placebo or control. In one trial, patients received light therapy as monotherapy or as adjunctive therapy to fluoxetine (Prozac). The pooled results of the 23 trials found that light therapy had a mild to moderate effect in improving depression symptoms compared with placebo or control (SMD = −0.45; 95% CI, −0.60 to −0.21; I2 = 57%). Subgroup analysis found that the bright white light subgroup had significant improvement with a small to moderate effect (20 trials; n = 973; SMD = −0.42; 95% CI, −0.64 to −0.20) and significant heterogeneity (I2 = 60%). The effects of the other types of light were no different from those in the control groups (three trials; n = 147; SMD = −0.25; 95% CI, −0.62 to 0.11; I2 = 14%). Subgroup analysis of the timing of therapy found that morning delivery had a moderately significant effect compared with the control group (18 trials; n = 843; SMD = −0.48; 95% CI, −0.69 to −0.21; I2 = 48%), whereas delivery at any other time was no different than in the control group (six trials; n = 277; SMD = −0.20; 95% CI, −0.63 to 0.23; I2 = 69.1%). Further subgroup analysis found that compared with the control group, treatment for less than 60 minutes per day had a moderate effect (eight trials; n = 381; SMD = −0.52; 95% CI, −0.78 to −0.26; I2 = 29.7%) and treatment for 60 minutes or more per day had a small effect (16 trials; n = 739; SMD = −0.36; 95% CI, −0.61 to −0.10; I2 = 63.6%). The overall findings of the study are limited by moderate heterogeneity (I2 = 56.9%). Recommendations from Others A 2010 evidence-based guideline from the American Psychiatric Association states that bright light therapy may be considered a low-risk, low-cost treatment option in patients with seasonal affective disorder or nonseasonal major depressive disorder.3 A 2015 American Geriatrics Society Beers Criteria update supports the use of bright light therapy as a low-cost, safe, and effective choice for older adults with nonseasonal depression.4 Page 16 Does community vision screening in patients 65 years and older reduce the prevalence of visual impairment? No, the available evidence does not support screening adults 65 years and older for visual impairment in the primary care setting. Among community-dwelling adults 65 years and older, vision screening produces no significant difference in the prevalence of visual impairment at follow-up compared with no screening. (Strength of Recommendation: A, based on a systematic review of randomized controlled trials [RCTs].) A 2018 systematic review and meta-analysis of 10 RCTs (N = 10,608) evaluated the effect of vision screening on the prevalence of visual impairment in community-dwelling patients 65 years and older.1 Patients were excluded for being too ill for assessment and living in a long-term residential care facility, although these criteria were not uniformly applied across studies. Screening methods included a vision questionnaire vs. no screening, visual acuity examination vs. no screening, and visual acuity examination as part of a detailed health assessment compared with a one-question vision assessment. The primary outcome was the degree of visual impairment as measured by patient self-report or visual acuity in the population at the end of each study period (range = one to five years total follow-up). In the subset of six studies comparing a vision questionnaire to no screening, the risk of “not seeing well” at follow-up was similar in patients who were screened and those who were not screened (six RCTs; n = 4,522; relative risk = 1.1; 95% CI, 0.97 to 1.1). Two of the studies comparing a visual acuity examination to no screening found no differences in near distance visual acuity at follow-up using a mean logMAR (Logarithm of the Minimum Angle of Resolution) chart, a standardized visual acuity chart similar to a Snellen chart (n = 653). A single study that evaluated a visual acuity examination as part of a detailed health assessment compared with a one-question assessment found similar risk of impaired vision (visual acuity worse than 20/63 in either eye) at three to five years (n = 1,807). All three comparisons had high-certainty evidence. In 2018, the Canadian Task Force on Preventive Health Care published an evidence-based guideline following a systematic review of 15 RCTs evaluating the effect of vision screening in a primary care setting for community-dwelling adults 65 years and older (N = 14,979; mean age = 78.5; 63% female).2 Nine of the 15 RCTs (n = 9,992) were included in the previous systematic review. The task force used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to determine the quality of evidence and strength of recommendation. Two types of vision screening were included (self-report of visual function using a questionnaire and objective visual acuity), and the comparison group received a visual assessment without active follow-up. Follow-up lasted 2.5 to 47 months (mean = 19 months) after the initial screening. Outcome measures addressed by the review were mortality, fractures, loss of independence, vision-related function, changes in visual acuity, quality of life, major adverse effects from treatment, and anxiety. In a subset of 10 RCTs reporting visual acuity, there was no difference in self-reported visual outcomes at a median follow-up duration of 20 months (n = 8,683; adjusted relative risk = 0.9% or nine per 1,000 persons screened; number needed to screen to prevent one case of low vision = 111; 95% CI, 16 more to 31 fewer vision issues reported). Evidence was judged as moderate quality. The guideline recommended against screening for impaired vision in primary care settings among community-dwelling adults 65 years and older with a weak recommendation based on low-quality evidence. Page 17 I see a middle-aged man who is noncompliant with levothyroxine therapy for hypothyroidism with a TSH level of 88 mIU per L. He recently visited an ophthalmologist for diplopia and was diagnosed with thyroid eye disease. The ophthalmologist recommended teprotumumab, which I'd never heard of. I learn that it reduces proptosis by blocking insulinlike growth factor 1 and decreases volume behind the eye. The patient has exophthalmos and disconjugate gaze and comments that he sees two of me. He is awaiting insurance authorization of the drug. I review records for a 73-year-old woman with diabetes mellitus who presented yesterday with severe pain in her right hand. She was unable to use her hand because pain radiated up her arm with any movement. Imaging shows chondrocalcinosis. This is her third episode of hand pain in four months. I had prescribed steroids for possible pseudogout; treatment was effective. However, I am reluctant to give her more steroids, so I prescribe colchicine for prophylaxis of acute pseudogout. I see a woman who was recently diagnosed with non–small cell carcinoma of the lung and had a right lower lobectomy. The patient received low-molecular-weight heparin subcutaneously after surgery, which caused thrombocytopenia, paradoxical thrombin release, and pulmonary emboli due to heparin-induced thrombocytopenia. She was treated with the direct thrombin inhibitor argatroban. Fortunately, she recovered and will be prescribed rivaroxaban for three months. I meet in person with my class of premed students at the University of Dayton, where I teach a medical terminology course. Several of the seniors have been accepted to medical school, and others are preparing to take the MCAT. I have missed my interactions with the students on our yearly medical brigades to Central America. I enjoy relating stories of diagnoses and patient presentations to help the students learn the language of medicine. I receive a call from a first-year resident who is caring for a 56-year-old man diagnosed with COVID-19 pneumonitis. The patient is on heated high-flow oxygen at 65 L per minute and will be moved to the ICU if he decompensates further. My next patient has a kidney stone. She doesn't want to be prescribed narcotics because of a previous opioid use disorder. I admire her decision while also worrying about controlling their pain. Fortunately, ketorolac and intravenous acetaminophen are effective. The patient with COVID-19 has become tachypneic and gone into atrial flutter. The intensivist agrees that it's time to transfer him to the ICU for intubation. The resident calls to inform his wife. She bursts into tears, telling us that two other family members who had the same exposure died last night. “I just can't believe how bad this is,” she tells the resident. I receive a message from my patient who has neuropathy of both feet and has developed a large ulcer that tracks to the bone on his right second toe. The podiatrist has decided the toe should be amputated and wants me to prescribe hydrocodone for postoperative pain. I let the patient know I will coordinate with the podiatrist, then chuckle when I realize he signed the last message, “Old Nine-Toes.” I get a call about an older patient with diabetes. Her chronic kidney disease had recently worsened, necessitating a switch from oral diabetic medications to insulin. The patient must give one of the insulin injections on her own, which is causing her significant anxiety. The home health nurse, clinical pharmacist, and I have been communicating with the patient three times per week to reassure her and adjust her insulin dose. I come home and my son asks me to play ball. We have some fun in the waning light before it's time for dinner. Page 18 Are older adults with coronary artery disease (CAD) at an increased risk of accelerated memory decline after coronary revascularization with coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI)? The study found no significant difference in the rate of memory decline among older adults with CAD who are undergoing coronary revascularization with CABG or PCI. (Level of Evidence = 2c) It is uncertain if the rate of memory decline in older people with CAD is changed after CABG or PCI. The investigators analyzed data obtained from a large prospective longitudinal survey of community-dwelling participants beginning in 1992 in the United States. Study participants included adults 65 years or older who underwent CABG, on pump or off pump, and PCI. As part of the study, participants took regular cognitive tests to assess longitudinal memory change. Analyses were adjusted for multiple potential confounders including age, education, financial assets, body mass index, smoking status, presence of daily pain or difficulty with activities of daily living, depression, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, stroke, heart disease, and race and ethnicity. The mean rate of memory decline was not significantly different before and after CABG or PCI. There was a statistically significant increase in the rate of memory decline after off-pump CABG compared with PCI, but not after on-pump CABG compared with PCI. The authors note that off-pump CABG is increasingly viewed as a less durable method of revascularization. Study design: Cohort (retrospective) Funding source: Government Setting: Population-based Reference: Whitlock EL, Diaz-Ramirez LG, Smith AK, et al. Association of coronary artery bypass grafting vs percutaneous coronary intervention with memory decline in older adults undergoing coronary revascularization. JAMA. 2021;325(19):1955–1964. Pharma marketing refers to the marketing of drugs and medical devices by private and public organizations to doctors, clinicians and consumers. With the average American spending $1,000 on drugs a year, marketing is a top priority for the major players in the pharmaceutical industry. With so much spending involved, most companies understand the great role and importance of marketing in pharma.But what makes pharma marketing so important?Well, marketing is now the key driving force behind shareholder value. More specifically, marketing enables pharma companies to identify, anticipate and provide solutions for customer requirements.At the same time, marketing is not always seen as a priority for pharma CEOs which is why professional marketers are often required to take responsibility for pharma branding and for the ROI on investment. While many people continue to view pharmaceuticals as commodities, marketers know that branding is the only way to help differentiate these companies from each other.In this article, we take a look at pharma marketing and what enables some pharma companies to stand out from the crowd.Taking a Closer Look – How Big is the Pharma Industry?The global market for pharmaceuticals is $900 billion and this figure is fully expected to exceed $1,1 trillions in the next few years. In fact, recent studies show the industry is growing at a rate of 5%, which is just behind the two other major healthcare segments – medical services and equipment.As a rule, drug affordability and disease prevalence continue to drive this rate, while government policies and regulation can impede or slow down this growth. However, it’s clear that this demand is not likely to slow down anytime soon and online trends can also attest to this statement.Either way, pharma is big business and one of the most in-demand and profitable industries in the world. That being said, how does one stand out or gain traction with so much competition?Does Pharma Spend More on Marketing than R&D?According to the NCBI, pharma companies spend approximately $2.6 billion for every drug they bring onto the market. For this reason, research and development will always impact the cost of a particular drug and this is also true when it comes to the costs associated with pharma marketing.In terms of the overall spend, most companies spend more on pharma marketing as opposed to research and development. For instance, Johnson & Johnson spent more than twice their R&D budget of $8 billion on marketing in recent years. As for the focus of these marketing efforts, pharma companies have a tendency to target physicians instead of the actual consumer.Now, while this might seem like a lot to the naked eye, pharma marketers are able to identify more than enough reasons to justify this large number. That is to say, relevant data and tools often indicate a much higher return on investment for pharma companies that invest in marketing as opposed to those who place less emphasis on it. And that’s just part of the story…READVerily Shelves Glucose-sensing Contact Lens ProjectWhat do Pharma Marketers Do Exactly?While studies show that most pharma CEOs believe new products to be the driving force of revenue, professional marketers think otherwise. The truth is, experts know that pharma marketing is more and more important as the differentiation between existing products becomes smaller. In fact, the key to growth in the pharma space is more closely associated with understanding consumer needs as opposed to creating or improving products.With this in mind, pharma marketers will place emphasis on identifying customer needs and finding solutions to meet these needs. Meanwhile, CEOs can focus on deploying their time and effort elsewhere, while knowing their pharma marketers can implement effective strategies for success.How to Market a Pharmaceutical productAs already mentioned, the gap between the features and benefits of pharma products is becoming less pronounced over time. When you think of it, this significantly reduces the impact of standard marketing efforts that focus on features and benefits. What’s more, the pharma industry is now highly commoditized which means that these products have less intrinsic value which in turn means that most pharma marketing deliverables are more or less the same from one company to the next.So how do you stand out of the crowd in pharma marketing?The answer is simple – Analytics based marketing.Rather than use the same “differentiators” as everyone else, savvy markets use certain drivers such as efficacy to stand out. When changing to analytics-driven methods, most marketers find the results are far more impressive than with taking a conventional approach. In short, data is now an important element for effective marketing and measuring these results is just as important.To this end, marketers can use analytics to measure effective marketing strategies and also to eliminate the risk of knee-jerk decision-making that might not produce a decent return on investment. In short, analytical decision-making can save both time and money for pharma companies.Needless to say, marketers must be able to prove that these methods are working and make changes in order to improve the bottomline. As a rule, marketing analytics metrics should include many factors including sales, costs and profits.Moral of the story: Branding is important but data analytics are needed to measure success. Also, marketing and revenue should be tied in order to produce the most desirable results.READAtomwise and Charles River Labs Form Alliance to Provide AI ServicesMarketing to Doctors versus Marketing to Patients: Differences & SimilaritiesPharma marketers have two audiences – patients and doctors. In terms of marketing strategy, it’s important to identify the most suitable audience and know the difference between them.As you know, consumers have a tendency to contact their local doctor for medical solutions or at least consult these individuals before purchasing a pharma device or prescription of some kind. Moreover, consumers are much more likely to buy with the recommendation of a doctor and this is certainly true if a certain device or prescription can be covered by insurance.When we take a closer look at the statistics, the average doctors in America has control over $2 million of healthcare costs every year which accounts for nearly 80% of the total spending countrywide. As a result, marketing to doctors is often more beneficial for pharma companies and different strategies are needed to address both doctors and patients.Let’s take a quick look at the difference between these two audiences and what pharma marketers might want to consider during the process.READPfizer puts a stop on its clinical studies for a potential DMD drugMarketing to DoctorsMarketing to doctors is all about identifying the needs of these professionals and providing well-researched solutions in a creative way through tactical media placement.Marketing to doctors is not cheap as competition and investment is high in this $450 billion industry. That being said, doctors hold the key to consumer sales and establishing a relationship with these professionals is a good way to communicate with a much wider audience.Here are some of the most important factors or considerations for marketing to doctors:Specific – Content marketing to doctors must be extremely specific to achieve results.Placement – Tactical placement is highly important to reach individuals who might be desensitized to traditional marketing strategies.Researched – Content Marketing must also be well researched and articulated in an appropriate manner.Unfortunately for many companies, most methods look the same when it comes to marketing to doctors and it must be known that there is often a reason for taking a conservative approach. However, creativity is essential in order to stand out as doctors are highly educated and most often desensitized to “savvy” marketing.Marketing to PatientsMarketing to patients is all about identifying individual needs and creating a patient experience that will provide efficient and specific value to address these same needs.Creating this patient experience is often an online process and one that relies heavily on strong search engine optimization and user experience. After all, patients are online nowadays and the statistics back this up.That is to say, most patients will now use search engines to find information or solutions relating to drugs, treatment, disease or other pharma issues. If companies can provide clear and efficient solutions to these search queries, this will inevitably impact sales and revenue.For example, most patients who suffer from depression will use a search engine to find medication for this condition. Statistics show that more than 2.5 million depression-related search queries are made every month and many of these keywords are yet to be targeted by pharma companies.With this in mind, if a pharma company creates a drug or treatment for depression, they can directly target the end-user through search engine optimization and content marketing in particular.How Pharma Marketers Think About Marketing to Doctors and PatientsMarketing has changed a great deal in recent years with most pharma companies starting to recognize the need for alternative strategies.It’s true, we live at a time in which people turn to their mobile devices for advice and price comparisons. Surveys show that one in twenty searches on Google are also health related and it’s not just consumers that use these engines but also the doctors who prescribe them.At the end of the day, patients and doctors are all consumers of information and pharma marketers must use known marketing strategies to build awareness and attract and convert these consumers.But what might this look like in the pharma industry?An Example of How a Pharma Company Might Market a ProductI like to learn by example. So let’s look at a very specific scenario. If we were the marketers behind Doxepin, a depression drug, it would make sense to create content around this particular drug which the end user is likely to find in search engine listings. Full disclosure: we’re not affiliated with Doxepin, we’re just using them as an example in this scenario. So how would we go about it? We might create robust content and marketing strategies that will communicate directly with the person searching for a solution to their depression. More specifically, we would use specific keywords, backlinking and organic marketing strategies to position this drug at the top end of search results for various depression-related queries.Now, in case this seems a little confusing, let’s take a simplistic look at the process: Analyze existing search results and identify commonly search keywords with low competition for depression medicine. Create articles about depression or this depression drug and insert selected keywords such as “best drug for depression” or “recommended drugs for depression” within this content. Publish this content on websites that have high authority and traffic. Create backlinks to these articles from other high authority websites. Continue to optimize the article until Google and other search engines rank this content on page one for the keywords that were identified for Doxepin.While this is a rather simple example and just one of many aspects of content marketing, you should see this investment is highly practical. However, research is essential and choosing the right keywords, links and strategies is always just as important as any amount of implementation. On the other hand, the effectiveness of this data and these efforts must also be measured, while certain changes will always be needed to make improvements to achieve the desired outcome.READSimon Stertzer on Driving Innovation in Cardiovascular InterventionFinal ThoughtsMarketing to patients and doctors require distinct strategies but pharma marketing in general involves the same principles that you find in any other industry. In many ways, implementing these strategies can take time due to lack of understanding and for the fact that many CEOs are still consumed by the ‘old way of thinking’.Either way, most companies are investing more in marketing than research and development for good reason but with most companies still implementing the same strategies, taking an alternative approach to marketing is most certainly the key to successful marketing in the pharma industry.