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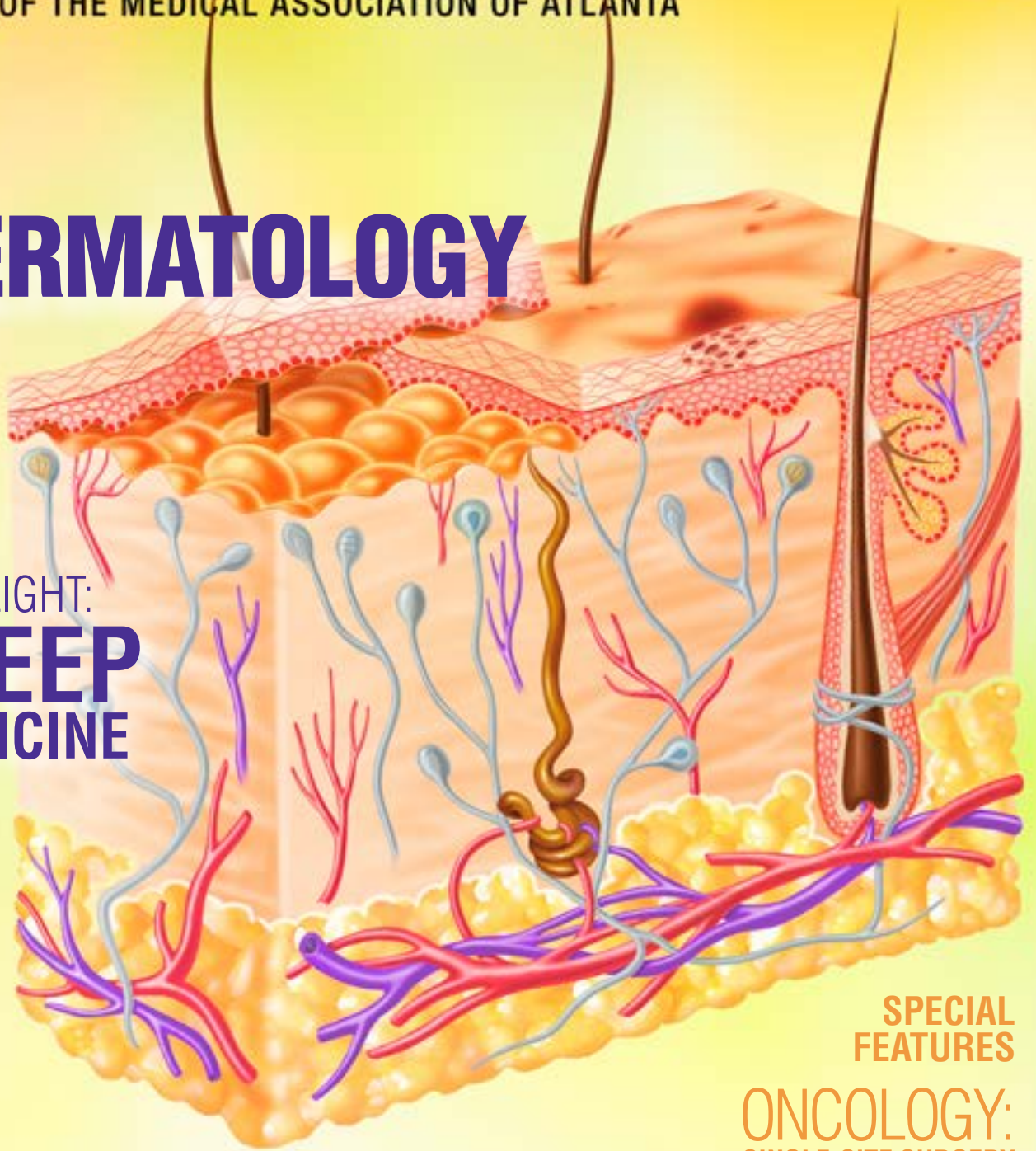
Medicine

2014 Vol. 85, No. 5

JOURNAL OF THE MEDICAL ASSOCIATION OF ATLANTA

DERMATOLOGY

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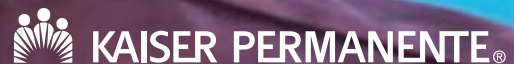
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Michael C. Hilton, MD, is in the private practice of general and forensic psychiatry in Atlanta, where he treats a wide range of adult psychiatric conditions. He is the 2012-2013 chairman of the Medical Association of Atlanta.

Nikhil Shah, MD, is the Chief of the Minimal Access and Robotic Surgery at Piedmont Health Care. He serves as the President and Founder of the Men's Health and Wellness Center of Atlanta.

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Lance Stein, MD, practices transplant hepatology at the Piedmont Transplant Institute. He serves on national committees for the American Association for the Study of Liver Diseases, American College of Gastroenterology and the American Society of Transplantation.

W. Hayes Wilson, MD, is a physician with Piedmont Rheumatology Consultants, PC. He has served as Chair of the Medical & Scientific Committee of the Arthritis Foundation and Chair of the Division of Rheumatology at Piedmont Hospital.



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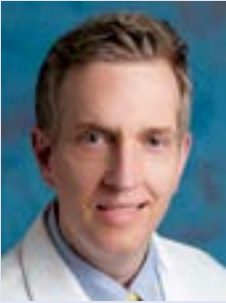
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GUEST EDITOR

**John Strickler, M.D.**

Dr. John Strickler is Chief of Dermatology for The Southeast Permanente Medical Group, which cares exclusively for Kaiser Permanente members in Georgia. A native of Atlanta, Dr. Strickler received his medical degree from Tulane University School of Medicine. He completed an Internal Medicine residency at Tulane and

his Dermatology residency at the Medical College of Virginia. He is board certified in Dermatology.

**Kenya H. Anders, M.D.**

Dr. Kenya Anders, board certified in dermatology and internal medicine, received her medical degree and dermatology training at the Medical College of Georgia. She has been serving members of Kaiser Permanente of Georgia as a dermatologist for 24 years.

**Asha R. Patel, M.D.**

Dr. Asha Patel practices dermatology for The Southeast Permanente Medical Group, which cares exclusively for Kaiser Permanente members in Georgia. She received her medical degree from the University of Miami School of Medicine and completed her dermatology residency at Columbia University/New York Presbyterian Hospital. She is board certified in dermatology.

**Helen Selser, M.D.**

Dr. Helen Selser practices dermatology for The Southeast Permanente Medical Group, which cares exclusively for Kaiser Permanente members in Georgia. Dr. Selser received her medical degree and completed her residency at the Louisiana State University School of Medicine. She also holds a master's degree in medical management and completed a fellowship in patient safety. She is board certified in dermatology.



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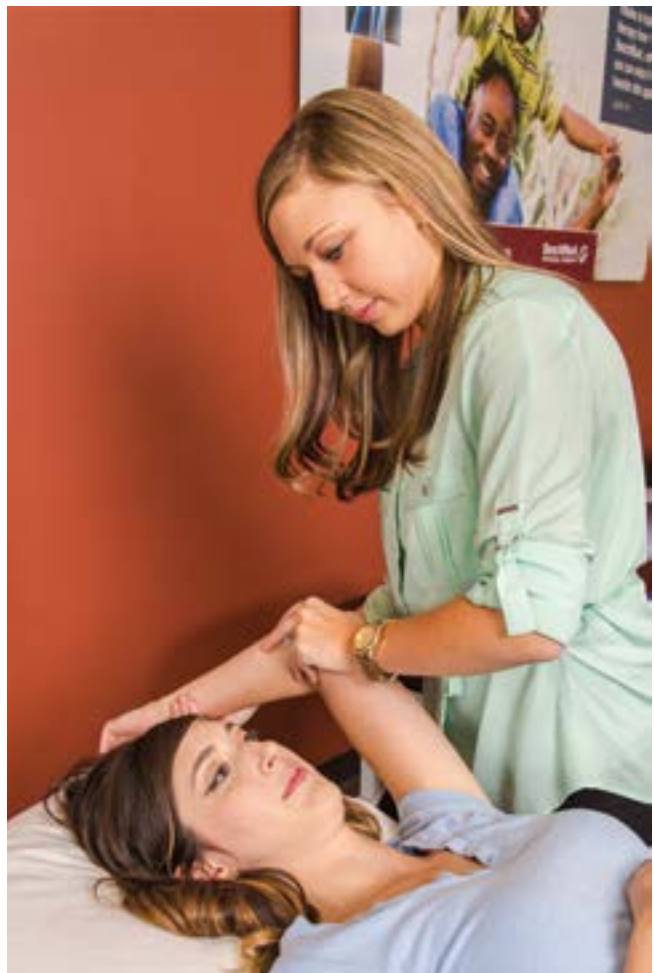
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DERMATOLOGY

Collaborating for the Best Patient Care

By John Strickler, M.D., MBA

The well-trained dermatologist must have a broad range of skills. These include expertise in pediatric dermatology, medical dermatology, dermatopathology and dermatologic surgery, including cosmetic dermatology. Collaboration with our primary care and other specialist colleagues in both the outpatient and inpatient settings is an integral part of our day-to-day work.

In addition to cutaneous malignancies and other surgical procedures, dermatologists have the specific training to manage conditions that include cutaneous lupus erythematosus, dermatomyositis and autoimmune blistering diseases, among others – diseases in which there are significant systemic manifestations and a need to use potent immunomodulating drugs.

The inpatient hospital dermatology consult can be helpful in diagnosing and managing patients being cared for by the medical and surgical teams. In this issue, Dr. Asha Patel discusses common skin diseases seen in hospitalized patients. Dermatologists are primarily office based and may not be able to be present in the hospital immediately, so recognizing morphologic patterns, as Dr. Patel discusses, is important in communicating with the dermatologist and developing a plan for managing inpatients.

Acute reactions like severe cutaneous drug eruptions are increasingly more common and likely to at some point confront physicians in every discipline. "The Update on Drug Eruptions" on page ten helps us recognize and triage these patients quickly to minimize the morbidity associated with these adverse reactions.

In "To 'D' or Not to 'D'," Dr. Kenya H. Anders tackles the somewhat controversial topic of Vitamin D from the perspective of the dermatologist. The official position of the American Academy of Dermatology (AAD) is that it does not recommend getting Vitamin D from sun exposure (natural) or indoor tanning (artificial), because ultraviolet (UV) radiation from the sun and tanning beds can lead to the development of skin cancer. Though this opinion is not shared by all disciplines of medicine, Dr. Anders' thoughtful exploration of Vitamin D gives some background and rationale for the AAD's position.

Dr. Helen Selser's review of nail fungus in the patient-centered medical home provides the current approach to the vexing problem of nail fungus. Choosing Wisely, a national initiative of the American Board of Internal Medicine (ABIM), stresses the need to be sure that there is confirmation via either culture, KOH or histology of nail fungus before embarking on treatment. Not all nail dystrophy is fungal, and Selser reviews some of the differential diagnoses that

need to be considered. Happily, there will soon be more effective topical treatment options for onychomycosis, and these are discussed in this review.

Like all medicine, dermatology is a vortex of change. Dermatology has always been a specialty with close ties between community and academic practice. We benefit greatly from this alliance with new and highly targeted therapies for cutaneous conditions, whether this be IL-12/23 blockers for severe psoriasis or prostaglandin D2's role in androgenetic alopecia.

Dermatology especially benefits from rapid advances in telecommunication technology. Teledermatology is quickly becoming an integral part of the day-to-day practice of our specialty. These advances will help us to continue to provide the highest quality and most cost-effective care for our patients and collaborate with our colleagues more conveniently and effectively. ■



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Pearls for Various Skin Manifestations

Dermatology More Than an Outpatient Specialty

By Asha R. Patel, M.D.



While primarily thought of as an outpatient specialty, the practice of dermatology also plays a vital role in certain hospital settings. By providing assistance for an efficient assessment, application of diagnostic studies and suggestion of treatment plans for cutaneous disease, the dermatologist can be a valuable asset to medical and surgical teams. Recognition of cutaneous manifestations of systemic disease is central to the consultant dermatologist's role and adds invaluable insight into perplexing diagnostic cases.

The following are clinical pearls relating to common dermatologic manifestations found in the inpatient setting. (For a discussion of serious skin eruptions secondary to medication reactions, see page 10.)

Erythema

Erythema, or redness of the skin, can have various presentations. Examples of causes leading to erythema include toxin-mediated erythema (bacterial/viral infectious etiology vs medication), Graft vs Host Disease (GvHD) or Kawasaki disease. Morbilliform eruptions (measles-like eruptions) are commonly due to drug eruptions, viral exanthems and GvHD. However, disseminated deep fungal infections such as histoplasmosis, cryptococcosis, and coccidiomycosis can also mimic the morbilliform pattern.

Erythroderma is defined as full-body erythema associated with skin scaling, also known as exfoliative dermatitis. There are numerous common and rare causes for erythroderma, such as drug reactions, psoriasis, cutaneous T-cell lymphoma

(CTCL), Sézary syndrome, atopic dermatitis, pityriasis rubra pilaris (PRP), systemic lupus erythematosus, pemphigus foliaceus, pemphigus vulgaris, seborrheic dermatitis, cutaneous manifestations of reactive arthritis, atypical pityriasis rosea, lichen planus, GvHD, diffuse histoplasmosis and nutritional disorders. Though literature reports suggest approximately 25 percent of erythroderma may also be idiopathic, some of these patients go on to develop CTCL and therefore should be monitored closely.

Management that is usually warranted in these cases includes a full body skin examination and diagnostic skin biopsies by a dermatologist for the underlying etiology. Diagnostic laboratory workup may be necessary on a case-by-case basis, but baseline labs – such as a complete blood count with differential, comprehensive metabolic panel and urine studies – are usually warranted at the time of the dermatology consultation.

Erythroderma is best managed in the inpatient setting, as these patients are prone to life-threatening systemic disorders such as thermoregulation from insensible water and protein loss, peripheral edema and tachycardia. Meticulous nursing care is of the utmost importance, as patients are also prone to skin breakdown and sepsis. Patients may also benefit from occlusion suits or extremity wraps over application of topical steroids. Communication between the hospitalist team, nursing team and the consultant dermatologist should be clear because of the complexity of care required.

“Cellulitis”

A great mimic of bilateral lower extremity “cellulitis” is acute venous congestion and venous stasis dermatitis. Patients with congestive heart failure, kidney dysfunction, hepatic disease, vascular disease and/or diabetes are more prone to this noninfectious cause of bilateral lower extremity erythema and edema. Supportive care, leg elevation, compression and treatment of the underlying systemic disease are recommended. Vascular surgery input may be necessary depending upon the clinical picture.

Cellulitic-like plaques that are a cause for concern include carcinoma erysipeloides, deep fungal infections (i.e. cryptococcus), and acute neutrophilic dermatoses

(aka Sweet syndrome). If plaques are ulcerating and/or not responding to standard antibiotic treatment, especially in the immunocompromised patient, these other etiologies need to be considered, which would require skin biopsies.

Necrotizing fasciitis, commonly known as flesh-eating bacteria, is obviously a life-threatening emergency and classically described as pain out of proportion to clinical exam with rapidly progressing edema, erythema, overlying bullae, cyanosis and eventually gangrene. Emergent surgical consultation for evaluation and treatment is necessary, with diagnostic blood cultures and tissue cultures at time of surgical debridement.

Other differential diagnoses that may appear to be similar to a “deep cellulitis” include panniculitis, diabetic muscle infarction and pyomyositis. A low threshold for radiologic imaging must be used as these can be quite serious and painful. Panniculitides may also need additional biopsies to elicit an etiology, based on the clinical exam.

Vesicles/Bullae

A presentation of generalized vesicles and bullae can be quite alarming, as this can represent serious infections or autoimmune blistering conditions. Varicella is one of the most common infectious causes of generalized vesicles, with the appearance of a classic “dew drop on a rose petal” appearance. Although this is classically seen in pediatrics, with the advent of varicella immunization, it is now common to see cases in adults that were once vaccinated. In patients who were vaccinated, it is common to see “abortive” cases of varicella, a milder presentation with shorter duration. Patients who are immunocompromised are also at risk for generalized varicella, even if they have already had primary varicella. Furthermore in pediatric patients, aspirin is an absolute contraindication in varicella cases as this may lead to Reye Syndrome.

Herpes simplex virus can also increase morbidity in certain situations. Lesions around the eye can lead to herpetic keratoconjunctivitis, which may lead to scarring and vision loss. In these cases, an urgent ophthalmology consult is warranted. Eczema herpeticum is a condition in which herpes simplex disseminates in a generalized distribution on compromised skin such as atopic dermatitis, pemphigus, Darier’s disease (DAR) or on burn patients. Treatment with oral or IV antiviral medication, depending on the extent of surface area involved and immune status, with meticulous wound care is necessary in these patients. Herpetic encephalitis is a severe complication of herpes when it affects the temporal lobes, presenting as decreased level of consciousness, seizures and fevers.

Autoimmune blistering conditions usually present as numerous and larger bullae and commonly require special

diagnostic biopsies for confirmation of diagnosis, such as a direct immunofluorescence (DIF) skin biopsy. Bullous pemphigoid (BP) is the most common autoimmune blistering condition with large tense bullae and typically presents in the elderly. Occasionally, urticarial plaques may precede the bullous stage of BP.

Components of the junctional adhesion complex within the skin and mucosa are targeted by specific circulating autoantibodies. There can be significant morbidity due to skin breakdown and resultant infection. Treatment is usually a combination of topical and systemic medications; these cases may necessitate a variety of immunosuppression, from corticosteroids to long-term steroid sparing agents.

Pemphigus vulgaris and pemphigus foliaceus are other autoimmune blistering conditions in which the autoantibodies are directed at cell adhesion proteins in the skin and sometimes the mucosa. These are more superficial than BP. Therefore, these bullae are more flaccid and may not even be clinically present; widespread erosions may be the only evidence of pemphigus.

These patients are also at risk for significant morbidity due to skin breakdown and resultant infection, and a treatment plan may be similar to a BP patient. However, as pemphigus can have debilitating mucosal findings, otolaryngology and ophthalmology colleagues may need to be involved to prevent long-term mucosal scarring and strictures.

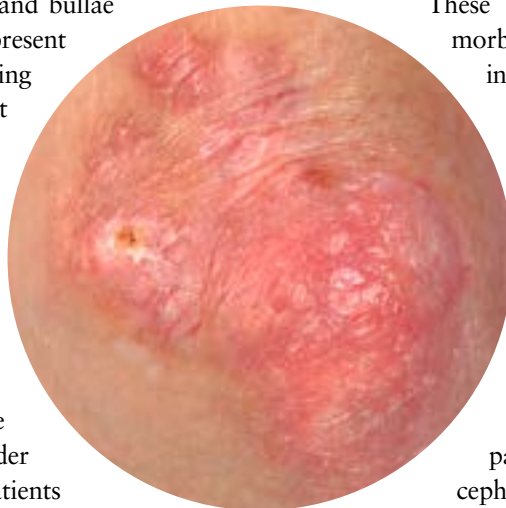
Linear IgA bullous disease is another blistering condition that may occur in the inpatient setting, as the adult form is essentially drug-induced, particularly in patients exposed to vancomycin. Penicillin, cephalosporins, ACE-inhibitors, and NSAIDs are also some well-known culprits.

It is thought that these medications stimulate a patient’s predisposed immune system to create IgA antibodies against specific proteins in the skin. Supportive care and withdrawal of culprit medications are key in management, with remission of eruption within two to six weeks of drug termination.

Pustules

Cutaneous pustules are a manifestation of a spectrum of dermatologic disease from drug eruptions, psoriasis, insect bites, contact dermatitis and various infections. Generalized pustules may herald a case of generalized pustular psoriasis (von Zumbusch variant). This is considered a dermatologic emergency and may require inpatient monitoring and systemic immunosuppression with cyclosporine, acitretin, or methotrexate. Intravenous steroids must be avoided, as this can exacerbate pustular psoriasis.

Generalized pustules in an immunocompromised patient may also be caused by disseminated candidiasis. These lesions may first appear as numerous erythematous papules with pale



centers, but typical pustular lesions may present later. The patient should also be evaluated by an ophthalmologist as eye findings, including candida endophthalmitis, can be present.

Disseminated gonococcal infection may also present as pustules in a febrile patient, but more classically localized over affected joints (i.e. knees, elbows, wrists, ankles). The pustules are larger, surrounded by erythema, and may be hemorrhagic. Gram stain cultures from the urethra, endocervical canal or posterior pharynx is usually the gold standard for diagnosis.

Papules/Nodules

Papules on the skin are common and have an innumerable list of differential diagnoses; most can be handled appropriately in the outpatient setting. However, if there is either a papule or nodule of a deep violaceous color (known as a “purple plum”), the differential is more of an urgent matter as diagnoses such as cutaneous metastases, lymphomas, melanoma, sarcomas, vascular tumors and vascular infections are more concerning. A skin biopsy is diagnostic, but in cases of unusual tumors it may take special staining and outside dermatopathologic consultation for a confirmatory diagnosis.

Immunocompromised inpatients may also be at risk for scabies; classic lesions are typically pruritic pink to skin-colored small papules on volar wrists, finger webspaces, peri-areolar and peri-umbilical skin. Scrotal papules are pathognomonic for scabies and can sometimes be the only finding.

Crusted scabies is typical of the immunosuppressed and appears as marked hyperkeratosis, particularly of acral sites. If a patient is found to have crusted scabies, hospital infection control may need to be involved as it is likely to have spread to hospital staff and patients.

Purpura (palpable and retiform)

Palpable purpura is typically a small vessel vasculitis issue, which has an array of etiologies such as infection, medications, systemic inflammatory conditions and malignancy. Histology is important to confirm the diagnosis, but a DIF skin biopsy may also be obtained for further etiology.

Laboratory testing, such as complete blood count with differential, comprehensive metabolic panel, urine studies, fecal occult blood test and a hepatitis panel, may be necessary for a thorough systemic work-up. Other testing such as a RPR, ANA, HIV, SPEP, UPEP, RF, Total complement/C3/C4, ANCAs, cryoglobulins and an up-to-date age appropriate



malignancy screening may also be necessary to tease out the etiology of the vasculitis if necessary.

Retiform purpura is more disturbing as it can quickly lead to necrosis of overlying skin.

Embolization or thrombosis of vasculature can cause the distinct retiform (netlike) pattern via intraluminal occlusion (extraluminal occlusion may also occur). Diagnoses to strongly consider are calciphylaxis, cryoglobulinemia or cryofibrinogenemia, septic vasculitis, severe acute meningococemia, levamisole exposure or a hypercoagulable state such as catastrophic antiphospholipid syndrome (CAPS). If one comes across periumbilical “thumbprint purpura” in an intensive care unit patient (usually on a respiratory vent), one must strongly consider hyperinfection of strongyloidiasis, which can quickly disseminate and lead to increased mortality. These cases are urgent and require quick diagnosis so treatment may be instituted.

Ulcers

Ulcers are commonly found in the inpatient setting and can be from a variety of conditions such as chronic venous insufficiency, a range of infectious etiologies and inflammatory conditions such as lichen planus or pyoderma gangrenosum. Chronic herpes simplex virus infections on the buttocks are very common in bedridden immunocompromised patients and should be cultured by the primary team. Ecthyma gangrenosum is another necrotic type of ulcer with raised erythematous borders classically associated with *Pseudomonas aeruginosa* bacteremia; these patients are critically ill and generally immunocompromised.

Pyoderma gangrenosum is a rare but chronic ulcerative disease that is usually associated with a variety of underlying systemic diseases. These can become large and painful with dusky borders and cribiform scarring; this requires a multidisciplinary approach with the involvement of a wound care nurse for management. Chronic non-healing ulcers, especially in venous stasis wounds or old burn scars, may need to be evaluated for a Marjolin’s ulcer, a squamous cell carcinoma that arises in previously traumatized and/or chronically inflamed skin. ■

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Update on Drug Eruptions: The Severe Cutaneous Adverse Reactions (SCARs)

By John Strickler, M.D., MBA

Early in our training, we learned the concept of *Primum Non Nocere* – First, do no harm. Unfortunately, today’s pharmacotherapy often has adverse cutaneous drug reactions – the leading cause of urgent dermatology consults.

While cutaneous reactions affect 2 to 3 percent of hospitalized patients, only a small minority (about 2 percent) fall into the category of Severe Cutaneous Adverse Reactions (SCARs). Early recognition and differentiation of SCARs from more benign drug eruptions or other skin conditions is necessary because discontinuation of the offending drug is the first, and most important, step in minimizing morbidity.

A majority of drug eruptions are morbilliform rashes that arise days to a week or so into therapy. Simple morbilliform eruptions are self-limiting and resolve over 5 to 7 days once the culprit drug has been stopped. Keep in mind that morbilliform eruptions may worsen before clearing after discontinuing the offending medication.

When a viable alternative therapy does not exist, continuing treatment in spite of a simple morbilliform drug eruption may be undertaken with close monitoring. A morbilliform drug rash may sometimes be a harbinger of a more serious reaction, and when this is the case, the rash is typically accompanied either concomitantly or by a prodrome of other symptoms.

Skin pain (as opposed to itching), fever, mucositis, blisters, facial edema, eosinophilia, elevated liver enzymes and deteriorating renal function are potentially ominous signs and raise the possibility of a SCAR. The “big” three SCARs include:

- Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN)
- Drug Rash (or Reaction) with Eosinophilia and Systemic Symptoms (DRESS)
- Acute Generalized Exanthematous Pustulosis (AGEP).

These distinct, but sometimes overlapping, reactions have several features in common: they are not easy to predict, not necessarily dose-dependent, affect a minority of patients and cause significant morbidity and sometimes even death.

For each of these SCARs, there are drugs that are more commonly associated and timing that is characteristic. Patients are often on multiple medications, making the culprit drug less obvious. Conditions like HIV and collagen vascular disease and underlying malignancy may predispose patients to SCARs.

Genetics also play a role. Certain HLA haplotypes are associated with particular SCARs and specific medications. Common genetic associations are abacavir and *HLA-B*5701*, allopurinol and *HLA-B*5801* and carbamazepine and *B*1502*. In fact, the abacavir package insert recommends screening for *HLA-B*5701* before initiating therapy with this antiretroviral.

Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN)

The spectrum of erythema multiforme (EM) historically included SJS along with EM minor and major. Current thinking places SJS and TEN into the same category. This is based on the mechanism and type of cutaneous damage found in SJS/TEN.

In SJS/TEN, there are several pathways leading to apoptosis of keratinocytes that lead to death and sloughing of the epidermis. EM minor and major are recurrent reactions most often resulting from infections (especially HSV and mycoplasma) and have a benign self-limited course. EM has the typical acraly located target lesions that may or may not blister. When mucosal involvement is present, it is usually the mouth and the conjunctiva and not severe.

In contrast, SJS/TEN begins with more centrally located slightly purpuric atypical targetoid plaques, which have a positive Nikolsky’s sign (light rubbing of the skin results in the formation of a blister). The extent of epidermal detachment

determines the category of SJS/TEN. In SJS there is less than 10 percent detachment of the body surface area, in TEN greater than 30 percent of the BSA, and SJS/TEN overlap between 10 and 30 percent.

The incidence of SJS/TEN, based on EuroSCAR data, is 1-2 per million. The incidence is higher in some groups like HIV patients, in which the incidence is as high as 1 in 1000. The incidence is increasing with the wider use of the most commonly associated drugs, like trimethoprim/sulfamethoxazole for MRSA, lamotrigine for mood stabilization and the new hepatitis C regimens.

SJS/TEN begins 1 to 3 weeks after the start of the offending drug. These patients are toxic and present with a prodrome of fever and malaise. Mucositis begins before skin separation by 24 to 48 hours. The skin sloughing rapidly spreads over 4 days, then tends to stabilize.

Many medications have been implicated in SJS/TEN. The common offenders are antibiotics (sulfonamides in particular), anticonvulsants, nonsteroidal anti-inflammatory drugs (NSAIDs), allopurinol and the antiretroviral drugs abacavir and nevirapine.

Antibiotics associated with TEN include the following:

- Sulfonamides (4.5 cases per million users per week)
- Macrolides
- Penicillins/cephalosporins
- Quinolones

Anticonvulsants associated with TEN include the following:

- Phenobarbital
- Phenytoin
- Carbamazepine
- Valproic acid
- Lamotrigine

TEN in patients on anticonvulsants may occur later in the course of the medication.

NSAIDs associated with TEN include the following:

- Oxicams (eg, piroxicam, tenoxicam) - Implicated more often than other NSAIDs

- Ibuprofen
- Indomethacin
- Sulindac

Hepatitis C treatment:

- Telaprevir
- Boceprevir

With allopurinol, risk is in the first few months of therapy. Reactions are more commonly seen in patients with renal insufficiency and especially when the allopurinol dose has not been adjusted.

The average reported mortality rate of SJS is 1 to 5 percent; TEN is 25 to 35 percent. Half of patients surviving TEN develop long-term sequelae, usually scarring of the skin, nails and eyes. A scoring system for the evaluation of TEN (SCORTEN) predicts mortality based on seven risk factors: age > 40 years, associated malignancy, heart rate > 120/min, epidermal detachment > 10%, BUN >27 mg/dL, serum glucose > 250 mg/dL and serum bicarbonate >20 mEq/L. Each category is either absent (0) or present (1). Mortality rates based on EuroSCAR data are as follows:

- Scorten 0-1 the mortality is >3.2 percent
- Scorten 2 the mortality is >12.1 percent
- Scorten 3 the mortality is >35.3 percent
- Scorten 4 the mortality is > 58.3 percent
- Scorten 5 the mortality is > 90 percent

Treatment of SJS/TEN is first and foremost the removal of the offending medication, followed by supportive treatment. Severe cases of TEN with 30 percent or greater BSA involved should be admitted, when possible, to a burn unit. These centers can manage fluid and electrolyte balance, nutrition, wound care and treatment of sepsis. In Atlanta, the Grady Hospital Burn Center is very skilled at managing these patients.

Care of the eyes should involve the ophthalmologist, as the application of amniotic membranes to the conjunctival surface is beneficial in minimizing ocular complications such as dry eye, scarring and, in rare cases, corneal perforation.



Typical morbilliform drug eruption.



Oral mucositis in a patient with SJS.



Facial edema in a patient with DRESS.

The use of the immunomodulators, IVIG and corticosteroids, in the treatment of SJS/TEN is not completely settled. Several studies have shown worse outcomes in those treated with corticosteroids primarily due to delayed healing and higher rates of sepsis. However, recent studies have demonstrated benefit in the immediate use of high-dose pulse methylprednisolone, especially in reducing the rate of ocular complications. Corticosteroids are used more commonly in patients with SJS than in patients with frank TEN.

IVIG is currently the most often used treatment in TEN. Antibodies in IVIG are able to block the process of apoptosis and halt epidermal damage. The recommended dosage is 0.75 to 1g/kg/day for three to four consecutive days in the treatment of SJS or TEN based on a meta-analysis of multiple case series.

There are no randomized controlled trials to assess the benefits and risks and to standardize the optimal treatment protocol (nor will these studies likely ever occur given the rarity of the condition and ethical implications). It is clear that if corticosteroids and/or IVIG are going to be used, doing so early in the treatment – within the first four days – and then stopping during the healing phase is necessary.

Drug Eruption with Eosinophilia and Systemic Symptoms (DRESS)

Drug reaction with eosinophilia and systemic symptoms (DRESS), is a severe multiorgan drug induced reaction. It begins with a viral syndrome-like febrile illness and a typically morbilliform rash, two to four weeks after initiation of the offending drug. DRESS can persist for weeks to months after the culprit medication has been discontinued.

Historically, DRESS has been known by several names, including anticonvulsant hypersensitivity syndrome and allopurinol hypersensitivity syndrome, but DRESS can be induced by multiple medications.

The reported mortality rate of DRESS is 10 percent. The cause of death is usually fulminant hepatitis.

DRESS begins with high fever and a rash, with the fever beginning first and the rash following a few days later. The rash most often is morbilliform but may be SJS-like with purpuric atypical targetoid plaques or generalized erythroderma. Cheilitis is also common and can cause confusion between DRESS and SJS. Facial edema is very characteristic of the reaction. Other conditions in the differential include staphylococcal scalded skin syndrome (SSSS), toxic shock, Still's disease and Kawasaki syndrome.

There are several proposed diagnostic criteria for DRESS, but no specific tests. The criteria are based on clinical and laboratory findings and include six criteria.

The first two criteria are necessary for diagnosis and include acute rash and the suspicion of a drug-related reaction. To establish the diagnosis, the patient should also have three of the four following systemic features: (1) fever >38°C; (2) lymphadenopathy involving at least 2 sites; (3) involvement of at least one internal organ (liver, kidney, heart, pancreas, thyroid or other organs); and (4) hematologic abnormalities, including a lymphocyte count above or below the normal limits; an eosinophil count higher than laboratory limits; or a platelet count below laboratory limits.

Lab testing and biopsy can be helpful in making the diagnosis, but are not specific. Reactivation of HHV-6 demonstrated by high titer IFA IgG or IgM helps in making the diagnosis, but there can be a significant delay in getting these results.

The lab work-up should include: complete blood cell count with diff, hepatic function panel, sodium, potassium, creatinine, eosinophil count, thyroid-stimulating hormone, blood culture and antinuclear antibody.

The overall population risk is between 1 in 1000 and 1 in 10,000 drug exposures, making it the most common of the SCARs. The drugs most commonly associated with DRESS

A majority of drug eruptions are morbilliform rashes that arise days to a week or so into therapy.

The mechanism of this systemic syndrome is thought to be the accumulation of reactive drug metabolites in patients with detoxification defects resulting in an immunologic reaction and/or the reactivation of Human Herpes Virus 6 with an overwhelming immune response.

The onset of DRESS is later and the duration of the reaction much longer than in other more banal drug reactions. The liver is universally involved, and there can be significant multisystem involvement, including renal failure, pneumonitis, myocarditis, pancytopenia and hypothyroidism.

include phenytoin, carbamazepine, lamotrigine, INH, phenobarbital, minocycline, allopurinol and sulfonamides, such as dapsone and sulfasalazine. There are rare but credible reports of many other drugs causing DRESS, including acetaminophen.

Discontinuation of the offending drug is the most important step. Systemic corticosteroids are used for more severe disease. The dose is 1mg/kg or the equivalent. Response can be rapid and dramatic but relapse upon tapering is common. These patients need to be monitored over months for relapse.

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When HHV-6 is known to be reactivated, Gancyclovir has been used as treatment, especially if there has not been a response to corticosteroids. Monitoring liver function, eosinophil count and creatinine is a good proxy for response to therapy. Other organ systems can be monitored clinically.

Because DRESS results from defects in metabolism, patients should be warned to avoid drugs of a similar class such as other aromatic anticonvulsants if there is a reaction to phenytoin. Family members are potentially at increased risk and should be cautioned about the potential risk with the class of medication that caused DRESS in their relative.

As the mechanism for these individual SCARs and genetic susceptibility become clearer, we will hopefully become better at predicting which chemical structures in which patients are more likely to induce a severe reaction.

Acute Generalized Exanthematous Pustulosis (AGEP)

Acute generalized exanthematous pustulosis (AGEP) is a specific skin reaction characterized by the sudden occurrence of dozens to hundreds of sterile, nonfollicular pinhead-sized pustules arising on an erythematous base. AGEP is often accentuated in the skin folds and reminiscent of pustular psoriasis.

Additional skin symptoms include edema of the face, as seen in DRESS, and dusky targetoid plaques seen in SJS. Mucositis can occur but is not severe and localized typically to the mouth. Fever, malaise and an elevated white count often accompany the skin findings. The incidence of AGEP is 5 per million annually. It is not common but is also under recognized.

The onset of AGEP is rapid, within a day to two weeks. The incidence of mortality is cited as 5 percent, but the vast majority of patients clear spontaneously over a week once the offending drug is removed. There are cases that eventuate into a TEN-like picture, and in these severe cases short-term corticosteroids are warranted. As healing progresses, the background erythema resolves and the pustules dry up followed by desquamation.

Beta-lactams and macrolides are the most common cause. Other drugs that reportedly cause AGEP include antifungals, particularly terbinafine, the usual anticonvulsants and calcium channel blockers.

Conclusion

The severity of these reactions and the fact that they seem to occur “out of the blue” inevitably raises the potential for litigation. Liability in these cases is based on informed consent and the appropriateness of the use of a drug for a particular indication. Common pitfalls include incorrect dosing of

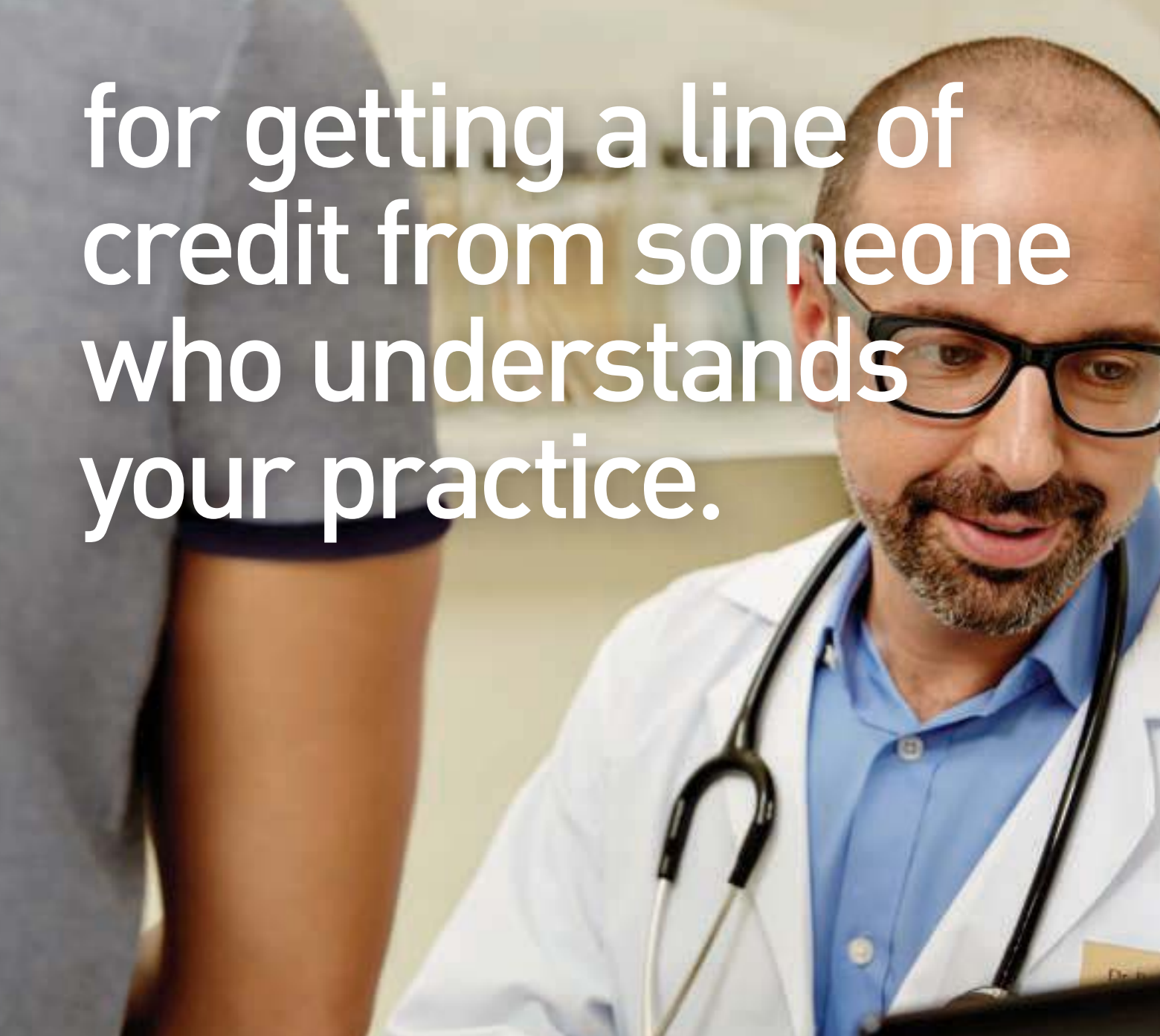
allopurinol in renal insufficiency or not slowly elevating the lamotrigine dose.

Was proper genetic pretesting done in the case of abacavir or in Asian patients being treated with carbamazepine? Did informed consent include the possibility of a SCAR when starting hepatitis C treatment or starting minocycline for acne?

There are notable drugs that more commonly cause these uncommon reactions. As the mechanism for these individual SCARs and genetic susceptibility become clearer, we will hopefully become better at predicting which chemical structures in which patients are more likely to induce a severe reaction. ■

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TO “D” OR NOT TO “D”

SHOULD YOU RECOMMEND VITAMIN D TO YOUR PATIENTS?

By Kenya H. Anders, M.D.

The human body requires Vitamin D to function, yet how we obtain the essential vitamin – and what we as physicians can safely recommend to our patients – is constantly up for debate.

DISCOVERY. Just one hundred years ago, rickets debilitated more than 80 percent of children living in New York City, Boston and London. In many northern cities, increasing industrialization, and the resulting factory work, shifted adults and children indoors, creating a disease not seen in the squalor of much poorer rural communities or cities of more equatorial climates.

By 1921, *JAMA* editorials touted cod liver oil as an effective antirachitic; scientists later isolated Vitamin D and recognized the connection to solar radiation. Two decades later, the USDA had instituted fortification of milk, breads and cereals. Rickets was largely eradicated, Vitamin D dropped off physician’s radar, and cod liver oil became a distant, distasteful memory.

Transportation and technology catapulted us into the age of trains, automobiles, air travel, indoor plumbing, electricity, radio, television, Hollywood, appliances, grocery stores, computers and the Internet – all of which made it more convenient, conducive, climate controlled and safer to work and play indoors.

DIET. Many physicians and patients assume that a well-balanced, vitamin-fortified diet is adequate to meet all

nutritional needs – including Vitamin D. Unfortunately, Vitamin D occurs naturally in only a few types of foods. The rest is naturally formed when sunshine strikes skin, cycling semiannually. (Figure 1).

Milwaukee-based Schlitz Brewing Company, maker of the now-defunct “Sunshine Vitamin Beer,” boasted in a 1936 ad, “As the summer sun heads south; as days grow shorter and stormier – we get less and less of sunshine’s benefits. Likewise, our ordinary foods are lacking in Sunshine Vitamin D, so essential to robust vitality. ... [Our beer] gives you the sunny source of health you need the whole year around ... and at no increase in price.”

DERMATOLOGISTS discourage deliberate ultraviolet radiation exposure; 90 percent of cutaneous malignancies are linked to cumulative and delayed effects of sun on our skin. Despite these efforts, one fifth of the United States (U.S.) population can expect to develop skin cancer in their lifetime. The National Cancer Institute estimates one death per hour from melanoma in the U.S. this year.

Figure 1

Food	per serving
• Cod liver oil (1T)	• 1360 IU
• Salmon (3 oz. cooked sockeye)	• 447 IU
• Mushrooms (1 cup diced portabello)	• 400 IU*
• Tuna fish (3 oz. drained)	• 154 IU
• Milk (8 oz. Vitamin D fortified)	• 120 IU
• Beef liver (3 oz. cooked)	• 42 IU
• Egg (one large with yolk)	• 41 IU
• Ready-to-eat cereal (1 cup fortified)	• 40 IU

*Can be increased several-fold by exposing caps to sunlight for several hours
Adapted from Office of Dietary Supplements, National Institutes of Health, 2013



Many risk factors for skin cancer are largely unavoidable (family history, natural skin pigmentation, history of childhood sunburns, altitude and latitude of residence) but lifestyle adjustments can limit ongoing exposure. These include staying inside during the middle of the day when the ultraviolet (UV) B rays are the most intense; avoiding tanning beds; wearing protective clothing, hats and glasses; and correctly applying (and reapplying!) a sufficient amount of sunscreen to exposed skin. In a December 2010 position paper, the American Academy of Dermatology issued a strong monition, warning that “There is no scientifically validated, safe threshold level of UV exposure from the sun or indoor tanning devices that allows for maximal vitamin D synthesis without increasing skin cancer risk.”



Figure 2

DEFENSE. The epidermis protects against solar damage and also makes Vitamin D3 for systemic use. Increased melanin content in the epidermis, either genetically directed or developed due to radiation damage as a tan, confers some barrier to penetration of longer wavelengths of light into the dermis. High concentrations of melanin also dampen Vitamin D synthesis in the skin so that darker complexions take longer to form the same amount of Vitamin D when compared to fair complexions exposed to the same intensity of light for the same amount of time.

DIFFERENCES IN LATITUDE. Figure 2 depicts rough, relative latitudes of countries and continents. Hundreds of years ago, before significant mass transportation, many people lived within walking distances of their ancestors’ habitats. Natives near the Arctic Circle, such as the Inuit of Alaska, tolerate months of complete darkness each winter, but their typical diet includes fish rich in Vitamin D.

Compare the latitude of the United Kingdom to that of Australia, used by colonial England as a penal colony. Australia’s indigenous peoples have darker complexions to compensate for their proximity to the equator, but, in general, the transplanted criminals did not, resulting in high rates of skin cancer that persist today. Compare also how much further north the United Kingdom is to the southern United States. The striking difference in latitude demands awareness and lifestyle accommodation for skin cancer prevention and subsequent Vitamin D supply.

DECIPHERING DOUBLES. There are two sources of Vitamin D: the sun and our diet. There are also two forms of Vitamin D supplements, D2 and D3, which are bioequivalent and handled identically by the GI tract. D2, a vegan source, is available in a prescription form of 50,000 IU; D3 – the form made in the skin – is the most commonly used over-the-counter supplement.

Both D2 and D3 have two names. D2 is also known as ergocalciferol; D3 is also known as cholecalciferol. Together they are

called calciferol. Supplements are dosed in either international units (IU) or in micrograms, with 40 IU equal to 1 microgram.

Vitamin D can be measured as two metabolites in the serum called 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D; 25-OH is the best form for screening and is the best marker of available bodily stores, working in concert with the parathyroid hormone to maintain calcium homeostasis. The 1,25-dihydroxyvitamin D form is complexly regulated and used to finesse levels in renal failure and sarcoidosis. (Figure 3) Test results are also given using two units. Most U.S. laboratories use ng/mL units for serum Vitamin D levels; others report using the international system of nmol/L. To convert from ng/mL to nmol/L, multiply by 2.5.

DISEASES. Vitamin D deficiency in infants is classically associated with rickets in children, osteomalacia and osteoporosis in adults. The distribution of Vitamin D receptors throughout the body, including in the brain, breast, prostate and macrophages, indicates a much wider role than in calcium homeostasis, including in autoimmune diseases, certain cancers and cardiovascular disease. It is hard to pick up a journal in any specialty without seeing ongoing studies of the effect of Vitamin D.

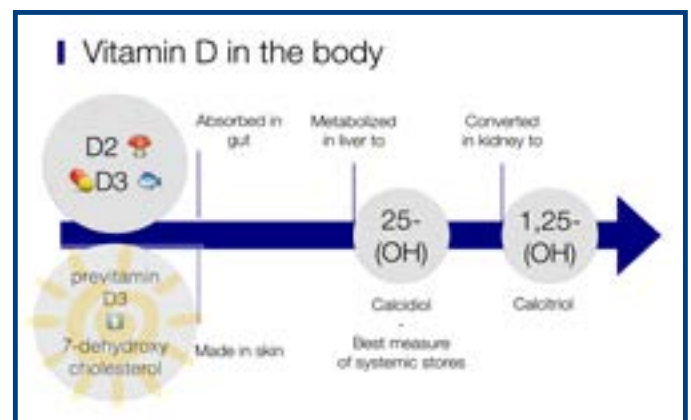


Figure 3

DETECTION. 25-hydroxyvitamin D blood levels (CPT code 82306) determine whether current supply is adequate. Fasting is not required. Medicare will not cover checking Vitamin D levels unless the patient has a documented Vitamin D deficiency or a limited number of diseases. (Figure 4) Consider testing – or perhaps empiric supplementation – in patients with those conditions or at increased risk of deficiency: people of color; who are elderly, obese or shut-ins; people on medications including anticonvulsants, HAART and cholestyramine; those with poor absorption due to inflammatory bowel disease, cystic fibrosis and celiac disease; and sun avoiders either due to cultural preferences or practicing “safe sun” for skin cancer prevention and anti-aging benefits.

DEFICIENCY DEFINED. Vitamin D levels are not static; they are highest in late summer and lowest in early spring, proportionate to the length and intensity (angle) of seasonal sunshine. The World Health Organization (WHO) defines 25-OH Vitamin D insufficiency as serum levels <30 ng/ml and Vitamin D deficiency if levels are < 20 ng/ml. Variations in Vitamin D binding protein levels in some people and certain medical conditions (malnutrition, liver disease) may affect the circulating levels.

Ideal levels and safe upper levels are still being discussed and studied. Some have suggested that African Americans have lower “normal” level than European Americans. However, a 2012 study from the British Journal of Nutrition revealed that Hadzabe and Maasai natives of East Africa, hunter-gathers wearing sparse clothes but avoiding sun during the hottest part of the day, had average levels of 44 ng/ml. Studies across eclectic populations including Hawaiian skateboarders, pregnant women on prenatal supplements, and resident physicians in Boston, Southern Brazil and India, show the majority (sometimes 80 percent or more) as Vitamin D deficient using WHO’s criteria.

DIGESTION. Vitamin D is absorbed in the distal duodenum and proximal jejunum of the small intestine. Patients with inflammatory bowel conditions, small bowel resection and bariatric surgery may need substantially higher supplement dosing. Food fortification will not be beneficial to people who avoid them due to lactase deficiency and/or gluten avoidance.

I Medical Necessity

- | | |
|-------------------------------------|----------------------------|
| • Deficiency, Vitamin D 268.9 | • Hypocalcemia 275.41 |
| • Disease, kidney, chronic 585.3-.6 | • Hypoparathyroidism 252.1 |
| • Disease, liver chronic 571.9 | • Malabsorption 579 |
| • Disease, bone, cartilage 733.90 | • Malnutrition 262 |
| • Disorders of calcium 275.40 | • Marasmus 261 |
| • Disorders of phosphorus 275.3 | • Osteomalacia 268.2 |
| • Hypercalcemia 275.42 | • Osteoporosis 756.53 |
| • Hyperparathyroidism 252, 588.81 | • Osteoporosis 733 |
| • Hypervitaminosis D 278.4 | • Rickets, active 268 |

Figure 4: Medical necessity codes for Vitamin D testing

Dosing compliance and intestinal absorptive capacity are the driving factors. For many adults, 1000-2000 IU a day may be sufficient, but for post-bariatric surgery obese patients, significantly higher doses may be needed. Toxicity has been reported but is rare.

DISCREPANCIES. The Kaiser Permanente Center for Health Research assayed Vitamin D supplements and noted a startling difference between the printed strength and the assayed activity (from 9 percent to 146 percent of the stated dose) of calciferol. The U.S. Pharmacopeial Convention (USP), an independent, nonprofit organization, annually audits voluntarily participating manufacturers of dietary supplements; approved Vitamin D products tend to test more closely to the stated dose than those from non-participating labs. Consider looking for the USP Verified Mark on supplement packaging to increase the likelihood of quality, potency and purity of the product.

DEBATE. “The devil is in the details.” More work needs to be done before we have a satisfactory solution to keep our patients and ourselves simultaneously protected from carcinogenic radiation while adequately providing for Vitamin D needs. We might have been spared this dilemma if our forefathers had not left the lands, latitudes and lifestyles of our ancestors. Personally, I prefer to stay in my current climate and maintain my mainly indoor lifestyle - even if I have to be mindful of the sun and Vitamin D. ■

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Diagnosing and Treating NAIL FUNGUS

By Helen Selser, M.D.

With an estimated 35 million cases each year, Onychomycosis (fungal infection of the nail unit) is one of the most common dermatological problems in the United States. While oral medications carry risks and often do not produce a lasting cure, new topical medications provide viable monotherapy alternatives.

Medical and consumer organizations are focusing on quality and safety in the diagnosis and treatment of nail fungus. The American Academy of Dermatology has collaborated with Choosing Wisely, a trademarked national initiative of the American Board of Internal Medicine (ABIM), to promote the most appropriate, cost-effective, evidence-based treatment. One of their five recommendations is to confirm nail fungus prior to starting oral therapy. This article will present information that may assist clinicians in diagnosing and treating this condition.

Types of Nail Fungus

It is estimated that only half of the cases diagnosed as fungal nails, and in some cases treated as fungal nails, are fungal. The other 50 percent of dystrophic nails are conditions that mimic fungal nails. Of the 50 percent that are fungal, 90 percent are dermatophyte. Ten percent are mold or other opportunistic organism. (Bologna)

There are several types of nail fungus:

Distal/lateral nail – commonly *T. rubrum*

Superficial white – often *T. metagrophytes*, cephalosporium, *Aspergillus*, *Fusarium* and, in HIV patients, *T. rubrum*.

Proximal subungual – less common and often with immunosuppression.

Destructive nail plate– with marked hyperkeratosis and often with paronychia involvement. This is seen in immunosuppressed cases or chronic mucocutaneous candidiasis. (Andrews)

Testing and Diagnosis

Dystrophic nails may appear as fungus, but a culture is needed to confirm fungus. No single method to confirm nail fungus provides 100 percent sensitivity. When a culture is taken, the dystrophic nail and subungual debris at the junction of the attached nail and nail bed must be submitted.

To obtain a nail culture, clip away loose nail plate and take the culture from the junction where the nail plate attaches to the nail bed. Having the proper tools to obtain this specimen is key. Many labs will accept nail clippings, so maintaining various media in the office is not necessary.

The nail plate may also be sent for PAS stain. This has a higher degree of accuracy (41-93 percent) than culture. Taking this sample requires a full thickness nail plate clipping. This does not require a biopsy of the nail bed, an invasive procedure. The sample is submitted to a pathology lab.

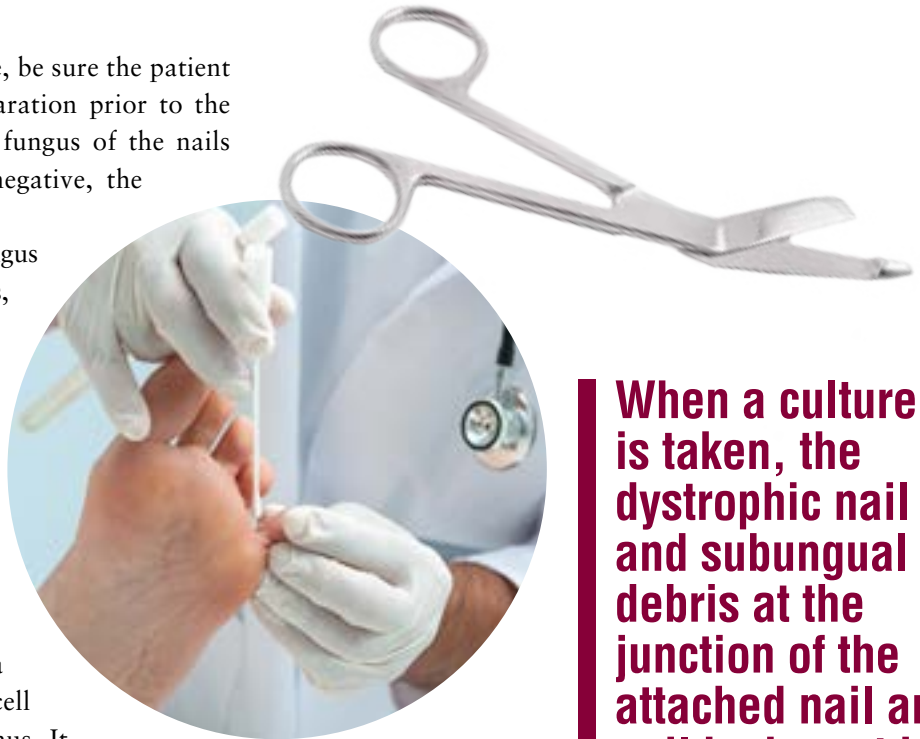
KOH shaving, which requires a very thin sample of the distal nail, is reported at 57 percent sensitive. The KOH result is impacted by collection technique and experience/training of the microscopic examiner.

The KOH and the PAS tissue stain confirm hyphal elements but cannot provide species identification. A fungal culture may provide species identification, but this may not add value to treatment. Additionally, KOH is an office procedure, while the PAS stain is a lab test. (Weinberg JM et al. *J Am Acad dermatog* 2003,49:193-197)

If the fungal culture returns negative, be sure the patient has not used topical antifungal preparation prior to the culture. Taking a second culture for fungus of the nails is helpful. If the second culture is negative, the problem may not be nail fungus.

The differential diagnosis of nail fungus includes psoriasis, lichen planus, squamous cell carcinoma, verruca, and other eczematous dermatosis. Squamous cell carcinoma is the most challenging and is a rare occurrence in dystrophic nails. It is more common in the fingernail than toenail, but does occur in both.

Periungual erythema and pain may be clues to squamous cell carcinoma. Onycholemmal carcinoma is a distinct type of squamous cell carcinoma arising from the nail isthmus. It is an indolent carcinoma confirmed by biopsy. (Chaser, BE, Renszel, KM, Crowson et al Oncholemmal



When a culture is taken, the dystrophic nail and subungual debris at the junction of the attached nail and nail bed must be submitted.



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carcinoma: A morphologic comparison of 6 reported cases. JAAD.2012.07.015)

If the nail culture is negative on two samples, consider a podiatry or dermatology consultation. If the nail is painful, bleeding or shows erythema, it may be important to send the patient for a nail bed biopsy.

Treatment

Treatment of nail fungus is challenging. The toenail grows slowly, only 1mm per month,



fully regrowing in 12 to 18 months. The fingernail may regrow in six months.

Oral medications are not always effective, have systemic risk and may interact with other medications. When informed of the risks, many patients decline treatment. Lab testing prior to, and during, treatment is recommended, based on the oral medication selected.

Pulse oral treatment may provide higher cure rates and reduced systemic risk. Treatment with oral medication has a high relapse rate. Clinical cure, where the nail appears normal, may not be confirmed by a mycological cure.

There are other considerations in treating fungal nails. The infected nails may infect others in the home. Studies have shown that the specific genetic type of *T. rubrum* infection is the same from adults with fungal infection in the same household.

There are new topical medications for fungus of the nail.

Efinaconazole 10 percent is the first topical triazole antifungal agent approved by the FDA. Tavaborole 5 percent is a boron-based benzoxaborole that has completed phase 3 trials.

Laser treatment with Nd:Yag is currently approved in the U.S. for temporary increase in clearing of nail fungus. The reports from randomized controlled trials do not show significant mycological or clinical clearance. (Hollmig, T et al JAAD 2013. 12.024 p911 923) ■

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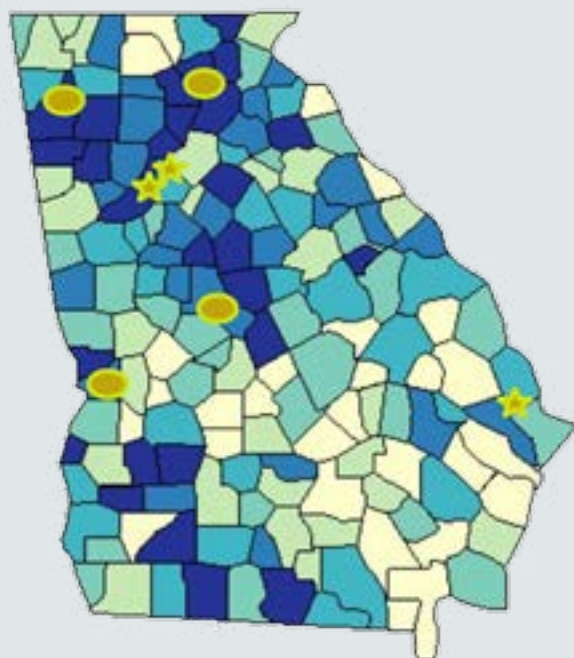
By Helen K. Kelley

A statewide initiative involving multiple hospitals and healthcare organizations is poised to bring the latest in cancer research and care to communities throughout the state of Georgia. This unprecedented partnership, sponsored by Northside Hospital Cancer Institute, was selected by the National Cancer Institute (NCI) as a NCI Community Oncology Research Program (NCORP). The designation includes a five-year, \$5.85-million grant.

The partnership application was developed jointly by Northside Hospital Cancer Institute and the Nancy N. and J.C. Lewis Cancer & Research Pavilion, part of St. Joseph's/Candler Health System in Savannah. Known as the Georgia NCORP, the partnership also includes the Georgia Center for Oncology Research and Education (Georgia CORE).

The Georgia NCORP will provide Georgians with access to state-of-the-art cancer prevention, screening,

Georgia NCORP Affiliates and Cancer Incidence by County



★ Partners

Northside Hospital Cancer Institute
 St. Joseph's/Candler Lewis Cancer & Research Pavilion
 Georgia Center for Oncology Research and Education

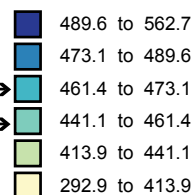
● Members

Harbin Clinic, Rome
 John B. Amos Cancer Center at Columbus Regional Health, Columbus
 Navicent Health Medical Center, Macon
 Northeast Georgia Medical Center, Gainesville

Age-Adjusted Cancer Incidence Rate

(Cases per 100,00)

Quantile Interval



US (SEER + NPCR)
 Rate (95% C.I.)
 453.7 (453.4 - 454.0)

Georgia
 Rate (95% C.I.)
 464.6 (462.5 - 466.6)

Map created by the Georgia Center for Oncology Research and Education with data from the National Cancer Institute State Cancer Profiles.

The community-based approach to cancer research has the potential to remove the barriers of location, age, ethnicity and economic status for all Georgia residents when it comes to accessing care.

control, treatment and post-treatment trials, with 110 oncology clinical providers in 41 different locations throughout the state, as well as the clinical trial leadership and research management services of Georgia CORE.

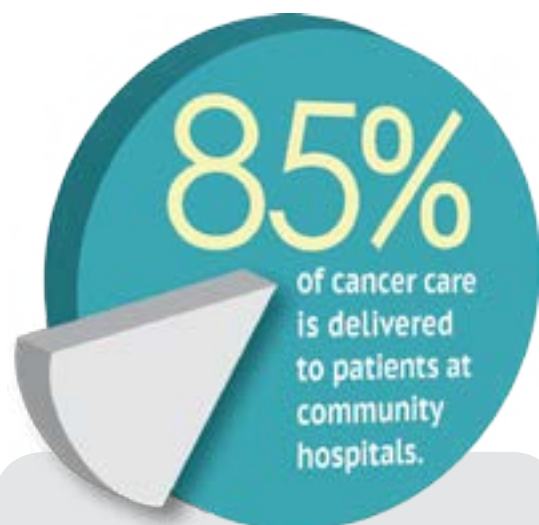
“Eighty-five percent of cancer care is delivered to patients at community hospitals, and only 15 percent at academic centers,” says Northside Hospital Cancer Institute’s Dr. Guilherme Cantuaria, who served as principal investigator for the partnership as it developed its application and will continue to coordinate the program. “The only way to improve delivery is by engaging our community healthcare facilities. Therefore, the overall goal of the Georgia NCORP is to bring cancer care and cancer delivery research to people right where they live.”

Tailored to Community-Specific Needs

Georgia NCORP will focus on offering research trials that address the needs of different communities, according to Dr. Cantuaria.

“All tumor sites will be studied, and all communities will be able to tailor the type of research trials they want to open according to their specific needs,” he says. “For example, Northside Hospital has a tremendous number of breast cancer and gynecological oncology patients. So it’s possible we’ll have more patients accrued to these trials as opposed to another community in Georgia that has a large population of smokers and high incidence of lung cancer.”

The purpose of customizing clinical trials by community is not only to identify the origin of various tumor sites, but also to identify the types of mutations exhibited by specific cancer cells and thereby develop the most successful treatments for those mutations.



According to the Centers for Disease Control and Prevention and the Georgia Department of Public Health:

- Georgia is ranked 25th in cancer incidence and 23rd in cancer deaths in the U.S.
- Cancer remains the second leading cause of death in Georgia.
- Prostate cancer accounts for 30 percent of new cancer cases, with the highest concentration in southwest Georgia.
- Breast cancer represents 31 percent of all new cancer cases, with the highest concentration in metro Atlanta.
- Lung cancer is the second most common among both males and females and is diagnosed most frequently in rural Georgia.

“We’re now in an era of genomic medicine, of targeted treatments. That’s where the NCI is going with this research,” says Dr. Cantuaria. “The latest clinical trials are focused on finding drugs that target specific cancer cell mutations.”

Improving Statewide Access to Cancer Research

While clinical trials and research are readily available to people who live in or near large urban areas, those who live in rural areas and less populated cities are not as fortunate.

“Historically, many of Georgia’s citizens have been challenged to find the cancer care resources they need – we have Atlanta ... and then there’s the rest of the state,” says Nancy M. Paris, president and CEO of Georgia CORE. “We’ve brought together

The Georgia NCORP will provide Georgians with access to state-of-the-art cancer prevention, screening, control, treatment and post-treatment trials, with 110 oncology clinical providers in 41 different locations throughout the state, as well as the clinical trial leadership and research management services of Georgia CORE.

strong cancer centers in Rome [Harbin Clinic], Columbus [John B. Amos Cancer Center], Macon [Navicent Health Center] and Gainesville [Northeast Georgia Medical Center] to create a collaboration of research as members of the Georgia NCORP in their own communities.”

In recent years, Georgia CORE participated in an opportunity with NCI to expand gynecological oncology trials throughout the state, creating a consortium of nine institutions. That experience, says Paris, proved that a collaborative effort could reach and fulfill an unmet healthcare need.

“This cooperative group within the NCI taught us that we can do more collectively than individually,” she says. “We learned that by expanding our resources to various centers and geographic regions, we are able to reach a broader, more diverse population.”

Based on its demonstrated effectiveness in working on NCI-sponsored studies, Georgia CORE was asked to provide clinical trial leadership and research management services as a partner in the Georgia NCORP.

“What we bring to the table is that we’re the mechanism by which cancer centers in Georgia have found ways to work together. We’ve conducted investigator-initiated clinical trials, and we’ve built a database in which all clinical trials and physicians and treatment centers in the state are listed as a resource for patients and professionals,” Paris says. “Georgia NCORP’s goal is to offer people the ability to get the best care at home. We’d love to see cancer patients look first at what’s available in Georgia, in their own communities.”

Importance of Community-Based Research

The NCI’s shift to community healthcare centers is significant, according to Dr. Cantuaria.

“For many years, the NCI focused on research at academic centers,” he says. “The community is the best place for testing the feasibility of new inventions and

new processes in the delivery of healthcare. And since the majority of cancer care is provided in the community, community-based research is very valuable – because it samples from a diverse, ‘real-world’ population, rather than a biased one.”

Howard A. Zaren, M.D., a surgical oncologist and

medical director for the Nancy N. and J.C. Lewis Cancer & Research Pavilion in Savannah, says that this change of focus brings an unprecedented opportunity for people who live in Georgia’s rural areas and smaller cities.

“Atlanta’s great for cancer care choices – if you happen to live there,” he says. “But if you live in smaller towns, there are no cancer physicians. So, this opportunity ... the forming of Georgia NCORP ... represents the first time that delivery of cancer care and research will be accessible throughout the state. That’s a huge change.”

Georgia NCORP will make clinical trials and cancer care available to previously underserved populations – groups that exhibit increasing incidence of cancer and experience socioeconomic depression – including the medically underserved, minorities, the elderly, women and young adults. The benefits of this partnership are far-reaching – researchers will have the opportunity to develop specific trials, measure their results, evaluate their success and tailor delivery of care within various communities. And cancer patients throughout Georgia will be able to take part in NCI-sponsored trials without having to travel long distances or leave their loved ones.

The community-based approach to cancer research has the potential to remove the barriers of location, age, ethnicity and economic status for all Georgia residents when it comes to accessing care.

“We’re passionate about making sure that Georgians can receive cancer care that’s as good or better than anywhere else. We’re in the top 20 states for cancer diagnosis in the country. We have a big incidence, and we have to take care of our population,” says Dr. Zaren. “The Georgia NCORP is a really big deal for us [as researchers and physicians] and a really big deal for patients in Georgia.” ■



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Photo by: Debra Jansen

SINGLE-SITE SURGERIES

And Expanded Services Address Full Continuum of Women's Oncology

By Helen K. Kelley

For many women, the prospect of a hysterectomy can be daunting, both physically and emotionally.

“So many women I knew who’d had hysterectomies warned me that I’d be in pain and unable to work or do much of anything for weeks and weeks after the procedure,” says Karine McMaster. “But my experience was nothing like that.”

McMaster, who underwent a hysterectomy in July, was moving around easily within a few days and was out of the house within a week of the procedure. She attributes this to a surgery that was performed with a single incision.

Margarett C. Ellison, M.D., recently performed McMaster’s hysterectomy at North Fulton Hospital using the da Vinci® Surgical System with Single-Site® technology. The single-site instrumentation allows the surgeon to remove the patient’s uterus and, if necessary, the ova-

ries and fallopian tubes through just one incision in the belly button.

Dr. Ellison, who has been performing traditional robotic surgeries with the da Vinci® Surgical System for several years, is one of the few surgeons in the metro Atlanta area currently using the single-site platform for hysterectomies. She says that although the single-site platform is a little more complicated, it works very well for patients with certain conditions.

“Although the single-site instrumentation is an extension of the robotic technology I was already using, it’s a little different. Single-site instruments are 5mm in diameter – much smaller and not as ‘hardy’ as traditional instruments – plus they are flexible, which has made some technical components of procedures more difficult and time-consuming from a surgical perspective,” explains Dr. Ellison. “But it was worth the learning curve for me,

because I believe there is a need and a niche for this type of surgery.”

According to Dr. Ellison, the single-incision procedure is an excellent alternative to a traditional hysterectomy for women with a genetic predisposition toward ovarian cancer or who have small uteruses or benign conditions such as endometriosis or uterine fibroids.

“For women with these types of conditions, a single-incision hysterectomy is less invasive with less blood loss and a lower rate of complications, and it offers a speedier recovery than traditional surgery,” she says. “In fact, most of my patients who have the single-site procedure are back at work in two to three weeks, versus the six-to-eight week recovery time required by an open procedure.”

Another benefit of the single incision is cosmetic. Rather than multiple abdominal incisions, women who undergo the single-site procedure have only a small, nearly undetectable incisional scar in the belly button.

“Improved outcomes and patient satisfaction, from both the surgical and cosmetic perspectives, are the driving forces behind offering single-site procedures,” Dr. Ellison says. “That’s the niche for this particular type of surgery.”

McMaster adds that if she ever faces a need for surgery in the future and has the choice of a single-site procedure, it’s a “no-brainer.”

“The single incision surgery was really amazing.”

Expanded Services Critical to IDing and Treating Women’s Cancers

In addition to bringing Dr. Ellison on board as gynecologic oncologist and developing a robotic surgery program that includes single-site procedures, North Fulton Hospital has expanded its entire women’s oncology program to encompass the full range of diagnosis and treatment options available.

“Our goal is to empower women by encouraging them to take care of themselves. And that includes getting regular physical exams and pap smears, as well as mammograms after age 40,” says North Fulton’s Oncology Services Manager Micah Brown, R.N. “So we’ve expanded our women’s oncology services in accordance with our mission of providing excellence in care.”

In addition to a multidisciplinary team of oncologists, surgeons, radiologists and staff members who are involved in the diagnosis, treatment and support of cancer patients, the hospital’s oncology services now include:

- An onsite infusion center, with staff trained and certified in chemotherapy
- An increased number of nurse navigators on staff to assist cancer patients throughout their continuum of care

- Screenings and treatments for the full range of gynecological and breast cancers

Brown says that physicians play a crucial role in helping their patients prevent or discover the early warning signs of cancer.

“It’s so important to encourage your patients to take care of their health by promoting healthy lifestyles and behaviors,” she says. “Part of that is motivating them to get regular checkups and screenings.” ■



Photo by: Debra Jansen

Check Up for Chicks: Why “It Matters”

Be there. For those who matter most.

That’s the message of Check Up for Chicks, North Fulton Hospital’s program that encourages women to improve their chances of living longer, healthier lives by getting regular screenings for cancer.

By logging on to www.checkupforchicks.com, women can find a wide range of information about different types of breast and gynecologic cancers. The site includes lists of risk factors and symptoms, answers to frequently asked questions, helpful videos and more.

Additionally, visitors can fill out a contact form or use the list of phone numbers provided on the site to find an appropriate physician or schedule screenings like a mammogram.



by Helen K. Kelley

SLEEP MEDICINE

by Helen K. Kelley

**Getting a good night's sleep
can be difficult for almost
half of the U.S. population**

Sleep disturbances and disorders can cause, and are often intertwined, with a myriad of health issues, including hypertension, diabetes, obesity and more. Physicians who specialize in sleep medicine evaluate, diagnose and manage conditions such as sleeplessness, sleepiness, fatigue and abnormal behaviors during sleep.

Sleep Disorders by the Numbers

Scott M. Leibowitz, M.D., a board-certified sleep medicine specialist with Laureate Medical Group, which has six metro Atlanta locations, cites the most common sleep disorders as classic insomnia, obstructive sleep apnea, circadian rhythm disorders, restless leg syndrome, narcolepsy and parasomnias. Many of these disorders, he says, are markedly common.

“Sleep problems can affect about 35 to 40 percent of the general population at any one time,” he says. “And there are certain populations in which we see an increase in the prevalence of sleep-related complaints.”

According to Dr. Leibowitz:

- Between 10 to 15 percent of the general population experience chronic insomnia, defined as difficulties falling or staying asleep with subsequent daytime symptoms such as fatigue or reduced cognitive function.
- The elderly have the greatest number of sleep-related complaints.

- Adolescents also have a significant number of sleep disorders.
- Women are at greater risk for sleep disorders than men.
- Roughly 40 percent of people age 60+ complain of insomnia or disrupted sleep.
- Sleep apnea is prevalent in post-menopausal women, and the incidence nears that of men at that same age.

Additionally, several diseases and conditions carry increased risks associated with sleep pathology, including heart failure, irregular heartbeat, hypertension, sleep apnea, stroke and diabetes.

Risky Business

Sleep deprivation poses health risks to people of all ages. Robert J. Albin, M.D., who specializes in pulmonary disease and sleep medicine with North Atlanta Pulmonary and Sleep Specialists, says that lack of sleep not only causes or exacerbates many health problems, but also affects critical thinking, which can influence a person's ability to judge risks and make decisions.

“Many accidents and man-made disasters have been linked to sleep deprivation. For example, Three Mile Island, the Exxon Valdez oil spill, Chernobyl, the tugboat accident in New York City ... these were all caused by someone who fell asleep at the switch or had impaired judgment,” he says. “There's a lot of speculation now about single car crashes –

that they may be related to sleep deprivation. Both quality and quantity of sleep can affect decision-making.”

Sleep performs several critical health functions, including repairing neural damage and consolidating thoughts and memories. Chronic sleep deprivation can result in decreased performance and alertness, memory and cognitive impairment, stress, reduced quality of life and even physical injury.

“Sleep is somewhat like rebooting or restoring a computer,” Dr. Albin says. “If we’re not sleeping well, we’re not repairing our hard drive properly.”

Targeted Treatments

While drug therapy, cognitive-behavior modification and CPAP and other mouth devices remain the primary treatments for sleep disorders, there are some new medications that hold promise for people experiencing sleep deprivation. These medications, such as Baclofen and Belsomra, allow for more targeted treatment of specific disorders.

Baclofen, a drug used to treat muscle spasticity for more than 50 years, is undergoing testing in mice by researchers at SRI International. Their findings show that Baclofen, which targets a deficiency of the neurotransmitter hypocretin, works better at treating narcolepsy than the best drug currently available for the disorder.

Belsomra (suvorexant) is a medication recently approved by the U.S. Food and Drug Administration for use as needed to treat insomnia. An orexin receptor antagonist, Belsomra is the first approved drug of this type. Orexins are chemicals that help regulate the sleep-wake cycle and play a role in keeping people awake. Belsomra alters the signaling of orexin in the brain.

Trending

Research suggests the growing possibility of a link between lack of sleep and obesity. In fact, a recent study conducted by MassGeneral Hospital for Children in Boston found compelling evidence that chronic sleep deprivation increases both obesity and adiposity in children as young as seven.

According to Dr. Albin, sleep abnormalities contribute to the abnormal regulation of neurohormones, which control appetite.

“Ghrelin is the hormone that signals hunger, and leptin is the hormone that signals satiety,” he says. “People with sleep disorders frequently have increased ghrelin levels and decreased levels of leptin, and the result is weight gain.”

Another growing trend in sleep disorders in both adults and children is related to technology. While it’s certainly not a new trend, Dr. Leibowitz says that sleep deprivation has evolved and escalated continuously since the invention of electricity.

“Everyone has an internal biological clock that determines his or her optimal window for sleeping and waking. Light has an affect on these circadian rhythms,” he says. “When

we introduce light that is in close proximity to our eyes – from sources like computers, cell phones and televisions – it signals our brains to suppress the output of melatonin, which is a hormone that is critical for regulating our sleep and wake patterns. So we can see a more pronounced delay in the sleep patterns of those people who are addicted to their technology.”

In the news: treating sleep apnea in cardiac patients reduces hospital readmission

A study of hospitalized cardiac patients is the first to show that effective treatment with positive airway pressure therapy reduces 30-day hospital readmission rates and emergency department visits in patients with both heart disease and sleep apnea.

Results show that none of the cardiac patients with sleep apnea who had adequate adherence to PAP therapy were readmitted to the hospital or visited the emergency department for a heart problem within 30 days from discharge. In contrast, hospital readmission or emergency department visits occurred in 30 percent of cardiac patients with sleep apnea who had partial PAP use and 29 percent who did not use PAP therapy.

The study results are published in the Oct. 15, 2014, issue of the Journal of Clinical Sleep Medicine, which is published by the American Academy of Sleep Medicine.

The study involved 104 consecutive patients who reported symptoms of sleep apnea while being hospitalized for a cardiac condition such as heart failure, arrhythmias or myocardial infarction. ■



Scott M. Leibowitz, M.D.



Robert J. Albin, M.D.

Common Associations with Sleep Problems The National Sleep Foundation’s 2003 Sleep in America poll shows that:

- Inadequate sleep is associated with diabetes in older adults.
- Sleep problems are common in older adults who are classified as obese or overweight.
- About one-half of older adults exercise three or more times a week to improve their fitness. The more that older people exercise, the less likely they are to report fair or poor sleep.
- 77 percent of older adults who are obese report some kind of sleep problem.



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This Month's Featured Board Members



Dorothy E. Mitchell-Leef, M.D.

Dr. Dorothy E. Mitchell-Leef is a reproductive endocrinologist and infertility specialist with Reproductive Biology Associates (RBA). She has practiced in Atlanta for 33 years. Prior to joining RBA, she was an Associate Professor at Emory in the Department of Ob/Gyn for 10 years. She served as President of MAA in 2000-2001 and has been on the board for 18 years. Dr. Mitchell-Leef received the Aven Citizenship Award from MAA in 2005 and the Health Care Hero Award and the Lamartine Hardman Cup from MAG in 2006. In 2013, she was awarded the Fellow in Medicine from the University of Louisville where she received her medical degree, residency and fellowship training. Her clinical interests include In Vitro Fertilization (IVF) for patients with general infertility needs, egg donation, fertility preservation and pregnancy loss with the need for genetic evaluation.



Lisa Perry-Gilkes, M.D.

Dr. Lisa Perry-Gilkes is an Atlanta-based Otolaryngologist who graduated from Spelman College, interned at Howard University College of Medicine and did her residency at Martin Luther King Jr. Medical Center in Los Angeles. She is board chair of the MAA, on the Medical Association of Georgia's board of directors, and also serves on the American Academy of Otolaryngology – Head and Neck Surgery (AAO&NS) board of directors.



Martha M. Wilber, M.D.

Dr. Wilber is a native Atlantan who has practiced with The Southeast Permanente Medical Group since 1989. She attended college at Harvard, and then returned home to complete medical school and an Internal Medicine internship and residency at Emory University School of Medicine. After completing residency, she spent an exciting year working as junior faculty in the emergency room at Grady, and then joined Kaiser Permanente. She is Board certified in both Internal Medicine and Palliative Care and her current clinical practice is as a hospitalist at Northside and Piedmont hospitals. Dr. Wilber is on the Board of Trees Atlanta, and of Georgia Watch, a consumer advocacy group that works to educate and empower consumers.

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