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INSIDE

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Mitochondrial Toxicity Associated with Linezolid

ABSTRACTS & COMMENTARY

By Dean L. Winslow, MD, FACP

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Dr. Winslow is a consultant for Bayer Diagnostics and Pfizer/Agouron, and is on the speaker's bureau for Pfizer/Agouron.

Synopsis: *Six patients developed lactic acidosis during prolonged linezolid therapy, possibly as the result of mitochondrial protein synthesis.*

Sources: Palenzuela L, et al. Does Linezolid Cause Lactic Acidosis by Inhibiting Mitochondrial Protein Synthesis? *Clin Infect Dis*. 2005;40: e113-e116; Soriano A, et al. Mitochondrial Toxicity Associated with Linezolid. *N Engl J Med*. 2005;353:2305-2306.

LINEZOLID IS AN OXAZOLIDINONE ANTIBIOTIC WHICH HAS proven to be very useful in the treatment of Gram positive bacterial infections, including methicillin-resistant *S. aureus* (MRSA). Its lipophilic properties and good penetration into pulmonary tissue allow it excellent activity in vivo in pneumonia due to MRSA, and its superiority to vancomycin has been demonstrated in clinical trials. While generally well-tolerated when given short term with prolonged therapy, myelosuppression (especially thrombocytopenia) is commonly seen. Less commonly, peripheral neuropathy and metabolic acidosis have been seen in linezolid treated patients.

Palenzuela and colleagues describe 3 patients who developed lactic acidosis while receiving prolonged linezolid therapy. Peripheral blood samples from these patients were examined by sequencing PCR fragments amplified from 12S and 16S rRNA, and direct sequencing of the PCR products was performed to identify known polymorphisms. To determine the frequency of polymorphisms in 100 control patients, restriction fragment length polymorphism (RFLP) analysis was performed using restriction enzymes to specifically identify the substitutions in question. One patient was found to have a homoplasmic A2706G in 16S rRNA,

Hospital Medicine Alert's physician editor, Kenneth P. Steinberg, MD, selected and reviewed the articles contained within this issue in July 2006.

one patient had a homoplasmic G3010A in 16S rRNA, and the third patient had no rRNA polymorphisms identified.

Soriano and colleagues also describe 3 patients who experienced linezolid-induced mitochondrial toxicity manifested by weakness and lactic academia. In all patients, mitochondrial respiratory chain complex II (succinate dehydrogenase, synthesized by cytoplasmic ribosomes) demonstrated normal activity in PBMC samples, but complex IV (cytochrome c oxidase, synthesized by mitochondrial ribosomes) activity was reduced.

COMMENTARY

Linezolid inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit and prevents the formation of the initiation complex which requires interactions with tRNA, mRNA, and the 30S ribosomal subunit.[1,2] Due to the similarities between the conserved domains of rRNAs in bacterial and human mitochondrial ribosomes, it is likely that linezolid causes mitochondrial toxicity by inhibiting protein synthesis. The 16s rRNA polymorphisms described by Palenzuela et al in 2 patients may confer genetic susceptibility to linezolid toxicity in a manner similar to the A1555G substitution in mitochondrial 12S rRNA, which confers susceptibility to aminoglycoside-induced hearing loss.[3] While chloramphenicol is seldom used now, older physicians were quite familiar with manifestations of mitochondrial toxicity associated with the use of this agent, which included anemia (which occurred commonly in patients treated for more than a few days) and the rarely seen grey baby syndrome of cardiovascular collapse in premature neonates associated with reduced metabolism of the drug. Chloramphenicol exhibits reversible binding to the 50S subunit of the bacterial ribosome at a locus which prevents the attachment of the amino acid-containing end of the aminoacyl-transfer RNA to its binding region.[4] Another class of antimicrobial agents commonly recognized as causing mitochondrial toxicities includes the nucleoside analogue HIV reverse transcriptase inhibitors, particularly the dideoxynucleoside agents. Nucleoside analogue toxicity is most commonly manifested by peripheral neuropathy, lipoatrophy, and less commonly by myopathy, encephalopathy, and hepatic steatosis with lactic acidosis.

Preclinical toxicity studies of linezolid performed by Pharmacia/Upjohn in rats and dogs, in retrospect, suggests mitochondrial toxicity, although specific studies to show this was the mechanism of toxicities observed were not performed. Myelosuppression was observed in both rats and dogs, which was time- and dose-dependent.[5] In addition, decreased food consumption, diarrhea, and mucosal histopathological changes (atrophy of intestinal mucosa and necrosis of crypt epithelial cells) were observed in rats. While not seen in the Pharmacia/Upjohn preclinical studies, the oxazolidinones were originally discovered by scientists at the DuPont Company, which advanced one compound, DuP 721, to Phase I clinical trials in the mid-1980s. Interestingly, the oxazolidinones were abandoned by DuPont in the late 1980s due to progressive fatal anorexia, which was seen in rats and dogs. My recollection is that nonspecific histopathologic changes similar to those reported by Pharmacia/Upjohn were seen in the DuPont preclinical pharm/tox studies. No mechanism of this was conclusively shown at that time but, in retrospect, it seems likely that this represented mitochondrial toxicity.

Due to its mechanism of action, it should not be surprising that linezolid is capable of causing mitochondrial toxicity. While linezolid is clearly an important drug for the treatment of antibiotic-resistant gram positive bacterial infections, clinicians should be aware of the potential for mitochondrial toxicity, particularly with prolonged therapy, and monitoring for myelosuppression and lactic acidosis should be routine. ■

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Questions & Comments

Please call Leslie Hamlin, Associate Managing Editor, at (404) 262-5416 or e-mail at leslie.hamlin@thomson.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

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Should Thrombolytic Therapy Be Used in Patients Older Than Age 80?

ABSTRACTS & COMMENTARY

By John J. Caronna, MD

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Dr. Caronna reports no financial relationship relevant to this field of study.

Synopsis: *The results of this study underline the uncertainty regarding the risk/benefit ratio of rtPA treatment in acute stroke in patients older than 80 years of age.*

Sources: van Oostenbrugge RJ, et al. Thrombolysis for Acute Stroke with Special Emphasis on the Very Old: Experience from a Single Dutch Centre. *J Neurol Neurosurg Psychiatry*. 2006;77:375-377; Schwark C, Schellinger PD. Is Old Age Really a Reason to Withhold Thrombolytic Therapy? *J Neurol Neurosurg Psychiatry*. 2006;77:289.

INTRAVENOUS RECOMBINANT TISSUE PLASMINOGEN activator (rtPA) is the only evidence-based specific treatment currently available for acute ischemic stroke. rtPA improved outcome in the NINDS Trial,[1] but it is unclear what the risk/benefit ratio is in very old patients. Therefore, van Oostenbrugge and colleagues sought to describe their clinical experience in 184 consecutive first-ever rtPA-treated patients at a single Dutch medical center. There was no upper age limit for eligibility. Stroke severity was assessed using the NIH stroke scale (NIHSS). There were no significant differences in stroke risk factors between the under and over age 80 years groups. Demographic data and time-to-treatment are tabulated (*see Table 1*).

Outcome was defined as favorable if the modified Rankin scale (mRs) score at 3 months was 0 to 1, and good outcome, functional independence, if the mRs score was < 2.

Seventy-four patients (40%) had a favorable outcome and 104 (57%) had a good outcome. Outcome at 3 months was related to age (*see Table 2*). Sixty-two (45%) patients < 80 years of age but only 12 (27%) patients > 80 years of age had a favorable outcome. The corresponding figures for good outcome were 88 (63%) and 16 (36%), respectively. The differences are statistically significant for both favorable and good outcomes.

Symptomatic intracerebral hemorrhage (SICH) occurred in 9 patients (5%), of whom 8 died. NIHSS scores and time-to-treatment were not significantly different in this group. Four patients (3%) with SICH were < 80 years of age and 5 (11%) were > 80 years of age. In 3 of 5 patients > 80 years of age, SICH occurred in areas not affected by acute infarction. In patients < 80 years of age, SICH occurred only in infarcted brain tissue.

COMMENTARY

van Oostenbrugge et al found a significantly worse outcome as measured by the mRS in patients older than 80 years of age compared to younger patients. The higher frequency of poor outcome in older patients could not be attributed to differences in baseline characteristics that are associated with worse outcomes, such as pretreatment hypertension, higher NIHSS score, or longer time-to-treatment. They found, as have others,[2] that besides stroke severity and preexisting disability, age is a strong and independent predictor of stroke prognosis.

van Oostenbrugge et al also found a non-significant trend towards more intracranial bleeding in older patients treated with rtPA. Therefore, they remain uncertain whether rtPA should be used in stroke patients over 80 years of age.

Schwark and Schellinger in an editorial commentary have no such uncertainty. Although they concede that older patients do have a higher risk of not recovering from ischemic stroke, they point out that this risk is not reduced by withholding thrombolytic

Table 1

Baseline Characteristics of Patients < 80 Years Treated with rtPA

	Age < 80 years (n = 139)	Age ≥ 80 years (n = 45)
Mean age, years	66	85
(median, range)	(68, 24-79)	(84, 80-97)
Men (%)	91 (65)	18 (40)
Pretreatment NIHSS Score n, (%)		
≤ 10	56 (40)	16 (36)
11-15	42 (30)	15 (33)
≥ 16	41 (30)	14 (31)
Time to treatment, min. mean ± SD	140 ± 34	148 ± 36

Table 2

Outcome Assessed by mRs Score at 3 Months

	0-1	2-3	4-5	Death
All (n = 184), %	40	25	13	22
Age < 80 years (n = 19), %	45	27	13	16
Age < 80 years, (n = 45), %	27	20	13	40

therapy. The elderly have a higher risk of complications from thrombolytic therapy. Therefore, physicians wishing to do no harm often do nothing at all. Schwark and Schellinger exhort physicians to take action and not to fear use of thrombolytics. They quote Arnold Schwarzenegger, "Fear is not an option" (from the film *True Lies*, 1994), but stop short of calling van Oostenbrugge and colleagues "girlie men."

Schwark and Schellinger agree that old age per se is not a contraindication to thrombolytic therapy in the elderly, until data from further randomized clinical trials indicate otherwise. ■

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When to Resume Full Activities After an Acute Myocardial Infarction

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

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Dr. Karpman reports no financial relationship to this field of study.

This article originally appeared in the May 2006 issue of Internal Medicine Alert. It was reviewed by the physician editor, Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD. Dr. Brunton is Clinical Professor at the University of California, Irvine. He is a consultant for Sanofi-Aventis and Ortho-McNeil. Dr. Roberts is Clinical Professor of Medicine at Albert Einstein College of Medicine. He reports no financial relationship relevant to this field of study.

Synopsis: *A return to full normal activities, including work at 2 weeks, after AMI appears to be safe in patients who are stratified to a low-risk group. This should have significant medical and socioeconomic implications.*

Source: Kovoor P, et al. Return to Full Normal Activities Including Work at Two Weeks after Acute Myocardial Infarction. *Am J Cardiol*. 2006;97:952-958.

THE MODERN ERA OF CARDIOLOGY IS A CONSTANTLY moving target. With respect to when patients who have suffered an acute myocardial infarction (AMI) should return to full activities and work, it is important to note the classic pathology study involving 72 patients published in 1939[1] by one of the giants of cardiology, Dr. Paul Dudley White. His detailed, critical, pathologic work revealed that

small infarcts were almost completely healed after 5 weeks and larger infarcts were completely healed after 2 months. As a result of this study, the founders of modern cardiology, such as Dr. Samuel Levine and even Dr. White, would keep their patients in bed for as long as 3 to 4 weeks before mobilization and discharge from the hospital. Of course, in the era of reperfusion therapy, management of patients with an AMI has changed dramatically and patients are now frequently discharged from the hospital within 3 days and usually return to work well within 6 weeks after the acute cardiac injury.[2-4]

Kovoor and colleagues from the University of Sydney in Australia, randomized 72 patients to return to normal activities at 2 weeks after an AMI and 70 other patients, who were treated with standard cardiac rehabilitation, were returned to normal activities at 6 weeks after an AMI. There were no deaths or episodes of congestive heart failure in either group and, in addition, there were no significant differences in the incidence of reinfarction, revascularization, left ventricular function, lipid levels, body mass index, smoking, or the results of exercise testing at 6 months after the AMI. They concluded that a return to full normal activities including work at 2 weeks after an AMI appeared to be safe in patients who were stratified to a low-risk group.

COMMENTARY

Returning to work as soon as possible after an AMI is critically important to patients in any occupation but especially to patients who are self-employed. Multiple, previously published studies have assessed return-to-work time after an AMI. From 1982 through 1984, the median time of return to work was 51 days to 2.27 months after an uncomplicated AMI.[3,5] In 1988, Topol and his group[2] reported that 86% of the patients in his early discharge group returned to work in approximately 41 days, whereas the vast majority of the patients in the conventional discharge group returned to work in 57 days. The randomized, controlled trial by Kovoor et al demonstrated that patients who were determined to be at low risk for future cardiac events after an AMI could return safely to full normal activities in only 2 weeks after the acute event, and that the accelerated return to normal activities did not increase the reinfarction rate, the need for revascularization, and did not negatively affect left ventricular function. It also should be noted that the lack of formal cardiac rehabilitation in the accelerated return to normal activities group made no difference in risk factors or exercise test performance at 6 months compared with patients who underwent formal cardiac rehabilitation activities.

It is now quite clear that appropriate risk stratification after an AMI can identify patients who are at low risk for future cardiac events. Larger prospective clinical trials are certainly needed. However, it would appear that it is quite safe to consider returning low-risk post AMI patients to full normal activities including work as early as only two weeks after the acute myocardial injury. ■

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Factors for Treatment Outcome in Acute Exacerbations of Chronic Bronchitis

ABSTRACT & COMMENTARY

By Joseph Varon, MD, FACP, FCCP, FCCM

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Dr. Varon reports no financial relationship to this field of study.

This article originally appeared in the May 2006 issue of Internal Medicine Alert. It was reviewed by the physician editor, Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD.

Synopsis: *The number of previous acute exacerbations of chronic bronchitis (AECBs) and the baseline FEV_1 level are potent prognostic factors of the short- and long-term outcomes of AECB.*

Source: Wilson R, et al. Antibiotic Treatment and Factors Influencing Short and Long Term Outcomes of Acute Exacerbations of Chronic Bronchitis. *Thorax*. 2006;61:337-342.

THIS MULTICENTER STUDY WAS AIMED AT EVALUATING the short- and long-term outcome of patients with

AECB treated with antibiotics. The study was designed as a prospective, randomized, double-blinded trial and was part of the MOSAIC study. Outpatients aged ≥ 45 years with documented chronic bronchitis were eligible for inclusion during an AECB-free period if they had a smoking history of at least 20 packs years, 2 or more documented AECBs in the previous year, and a forced vital capacity in one second (FEV_1) of < 85% of predicted at the enrollment visit. Patients were then randomized to received either moxifloxacin (400 mg daily for 5 days) or one of the following comparators: amoxicillin (500 mg three times daily for 7 days), clarithromycin (500 mg twice daily for 7 days), or cefuroxime-axetil (250 mg twice daily for 7 days). Clinical response was evaluated 7-10 days at the end of the treatment. Factors with potential impact on the clinical outcomes studied included: age (> 65 or < 65 years), body mass index (< 30 kg/m^2 or > 30 kg/m^2), gender, co-morbidities, number of AECBs in the previous years (severity of chronic bronchitis), concomitant medications and FEV_1.

Seven hundred-thirty patients were studied. The mean age was 63.2 ± 9.8 years; 43.2% had an FEV_1 < 50% and 27.7% had ≥ 4 exacerbations the previous year. Moxifloxacin was independently associated with a higher cure rate than the comparator drugs while co-morbidities, FEV_1, 50% predicted, and ≥ 4 AECBs in the previous year had a detrimental effect on the outcome.

Once adjustments were made, in univariate analysis, the factors that had a significant impact on the occurrence of the composite event were ≥ 4 AECBs in the previous year, age > 65 years, FEV_1 < 50% predicted and acute bronchodilator use had a statistically significant effect on long-term outcome. The effect noted for moxifloxacin was primarily linked to benefits in the subgroup of patients aged > 65 years.

COMMENTARY

AECBs are commonly seen in primary care practices worldwide. This study is interesting because it reaffirms that the severity of airflow obstruction, coexistent comorbidities (such as cardiac disease) and the frequency of exacerbations are risk factors for poorer short-term outcomes in AECB.

A number of studies in the past decade have shown similar results in patients with AECB.[1-3] Ball and coworkers have demonstrated that a past history of frequent exacerbations makes a future exacerbation more likely.[4] This is perhaps because the index exacerbation is not completely resolved and these patients tend to have persistent bacterial infection. Aggressive antibiotic treatment is therefore justified in patients meeting criteria. It is interesting to note that among the agents studied, moxifloxacin had a beneficial effect in the short- and long-term outcome, despite presence of other negative prognostic factors. ■

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Cleansing Patients with Chlorhexidine Promotes Infection Control

ABSTRACT & COMMENTARY

By Leslie Hoffman, PhD, RN

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Dr. Hoffman reports no financial relationship to this field of study.

This article originally appeared in the May 2006 issue of Critical Care Alert. It was reviewed by the physician editor, David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, and Dr. Thompson is Staff Pulmonologist, VA Medical Center, Associate Professor of Medicine, University of Washington. Dr. Pierson and William Thompson report no financial relationships relevant to this field of study.

Synopsis: *Cleansing patients with chlorhexidine-saturated cloths reduced VRE contamination of patients' skin, the environment, and health care workers' hands, and also decreased VRE acquisition.*

Source: Vernon MO, et al. Chlorhexidine Gluconate to Cleanse Patients in a Medical Intensive Care Unit: The Effectiveness of Source Control to Reduce the Bioburden of Vancomycin-Resistant Enterococci. *Arch Intern Med*. 2006;166:306-312.

INFECTION CONTROL PRACTICES OFTEN TARGET CLINICIAN behaviors, eg, improving adherence to hand washing

hygiene and other infection control practices. This study tested an alternative approach: source control. Over a 15-month period, all patients (n = 1787) admitted to a medical intensive care unit (MICU) were bathed during three sequential periods with soap and water (Phase 1), single-use, no rinse disposable cloths saturated with 2% chlorhexidine gluconate (Phase 2), and single-use, no rinse disposable cloths without chlorhexidine (Phase 3). Each study phase lasted for approximately 5 months. The study used a standard set of bathing procedures and products, eg, Dial soap (Phase 1), packets containing 2 non-medicated cloths for face and neck cleansing and 6 medicated cloths for body cleansing (Phase 2) and packets containing a similar number of non-medicated cloths (Phase 3). Vancomycin-resistant enterococci (VRE) acquisition was defined as a positive finding for VRE on a rectal culture specimen > 3 days after MICU admission with at least 1 prior negative culture.

Compared with soap and water, bathing patients with chlorhexidine-saturated cloths resulted in 2.5 $\log_{10}$ less colonies of VRE on patients' skin and less VRE contamination of health care workers' hands (risk ratio [RR], 0.6; 95% confidence interval [CI], 0.4-0.8) and environmental surfaces (RR, 0.3; 95% CI, 0.2-0.5). The incidence of VRE acquisition decreased from 26 colonizations per 1000 patient-days to 9 per 1000 patient-days (RR, 0.4; 95% CI, 0.1-0.9). For all measures, the effectiveness of cleansing with non-medicated cloths was similar to that of soap and water baths. Skin condition was assessed daily. More patients had deterioration in skin condition during soap and water bathing compared to chlorhexidine (P = .02) or nonmedicated cloth (P = .001) bathing.

COMMENTARY

Today we face an ever-increasing number of pathogenic bacteria with diminishing susceptibility to antibiotics. Commonly, approaches to reducing cross-contamination with resistant bacteria such as VRE have focused on improving adherence to infection control recommendations. This study evaluated a different approach—source control. The goal was to reduce microbial skin density and, thereby, patient-to-patient transmission. Chlorhexidine was selected because of its low toxicity and known effectiveness against a broad range of pathogens. To detect VRE hand carriage, culture specimens were obtained from a convenience sample of individuals exiting rooms of patients with VRE colonization and from individuals in common MICU areas. To detect environmental contamination, specimens were obtained from the bed rail, pull sheet, and overbed table.

Daily bathing with chlorhexidine produced lower bacterial counts on patients' skin, hands, and surfaces. With such an intervention, there are always concerns about development of resistant organisms and skin reactions. Resistance, evaluated using median chlorhexidine inhibitory concentrations for strains of VRE (11 strains of *Enterococcus faecalis* and 52 strains of *Enterococcus faecium*) was similar during each phase. Also, there were no adverse reactions in the 642 patients enrolled in the phase with chlorhexidine bathing. To avoid the potential of allergic reactions, the bathing procedure did not involve use of chlorhexidine on the patients' faces. Skin condition for most patients (89%) was unchanged and deterioration was more common during soap and water bathing and bathing with nonmedicated cloths. However, mean MICU stay was only 3.4 days and findings might have differed if the intervention was applied to long-stay ICU patients.

Findings of this study provide strong initial support for bathing with 2% chlorhexidine gluconate as a measure to reduce the transmission of VRE in high-risk settings such as the ICU. Studies involving a longer observation period are needed to evaluate safety and efficacy in long-stay ICU patients. ■

Is There Something About Air Travel Besides Immobilization that Increases Risk of DVT?

By Louis Kuritzky, MD

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This article originally appeared in the May 2006 issue of Internal Medicine Alert. It was reviewed by the physician editor, Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD.

THAT DEEP VENOUS THROMBOSIS (DVT) CAN OCCUR AFTER air flight is not a new observation, having been first reported in the 1950s. Recent data have singled out very long flights (8 hours or greater) as being remarkably more important for DVT risk than shorter flights.[1] Generally, risk for DVT with air flight has been simply attributed to only one of the 3 characteristics of Virchow's Triad: stasis (due to immobility). Schreijer and colleagues studied the impact of clotting factor activation associated with air flight.

To differentiate simple immobilization on the ground, from immobilization with air flight, study subjects were divided into 3 groups: a real 8-hour plane flight, an 8-hour period of immobilization while watching successive movies, or the control of 8 hours of normal daily activities. The 71 men and women participated in 2 cross-over periods, so that all subjects experienced all 3 group activities.

Several coagulation factors were monitored. After flight, thrombin-antithrombin complex was elevated (indicating increased thrombotic activation), but not after 8 hours of movie immobilization or daily activities. Coagulation activation was most marked in women on oral contraceptives who had known factor V Leiden at baseline. Schreijer and colleagues postulate that the hypobaric hypoxia encountered in flight explains the coagulation activation. Advice to avoid protracted immobility on long flights can be helpful, but may not be fully protective, since other mechanisms in addition to immobility appear to be etiologic. ■

Reference

1. Schreijer AJ, et al. Activation of Coagulation System During Air Travel: A Crossover Study. *Lancet*. 2006; 67:832-838.

The Dermatologic Nikolsky Sign: How Good is it?

By Louis Kuritzky, MD

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Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

This article originally appeared in the May 2006 issue Internal Medicine Alert. It was reviewed by the physician editor, Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD.

PV NIKOLSKY WAS A RUSSIAN DERMATOLOGIST WHO published information about *Pemphigus foliaceus* in 1896. He was the first to describe an altered structural integrity of the epidermis in pemphigus. The Nikolsky Sign (also commonly spelled Nikolskiy) is performed by placing pressure upon skin adjacent to tissue involved with bullae. In pemphigus, because the attachments of the intraepidermal intercellular bridges are damaged, skin pressure will allow the bulla to dissect further within the epidermis, as the layers separate due to IgG-mediated attachment defects. Although at one time considered specific to pemphigus, Nikolsky Sign has been sometimes reported in association with other skin disorders, such as toxic epidermal necrolysis, mycosis fungoides, and epidermolysis bullosa.

To study the sensitivity and specificity of the Nikolsky Sign, patients (n = 127) with a variety of bullous lesions were tested. The sensitivity for diagnosis of pemphigus by Nikolsky sign was only 38%.[1] Disorders other than pemphigus also manifest Nikolsky sign. A positive Nikolsky sign is useful to support the diagnosis of pemphigus, but is also seen in other disorders. ■

Reference

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CME Questions

10. In the Vernon et al study, cleansing patients in the medical ICU with a cloth medicated with 2% chlorhexidine resulted in:

a. increased skin irritation for patients and health-care workers.
b. a decreased number of patients who acquired VRE.
c. increased rates of nosocomial bacteremia due to MRSA.
d. decreased mortality rates.
e. no observable benefit.

11. The use of rtPA in patients over the age of 80 years who resent with an acute ischemic stroke:

a. is contraindicated.
b. increases the risk of intracerebral hemorrhage.
c. increases the likelihood of a favorable outcome.
d. decreases the likelihood of a favorable outcome.
e. has an unclear risk/benefit ratio.

12. Factors that were predictive of a poor prognosis after an acute exacerbation of chronic bronchitis in the study by Wilson et al included all of the following *except*:

a. Body mass index
b. Severity of underlying airflow obstruction
c. Coexistent comorbidities
d. Frequency of exacerbations in the previous year
e. Age

Answers: 10. (b); 11. (e); 12. (a)

CME Objectives

The objectives of *Hospital Medicine Alert* are to:

• review pertinent safety, infection control, and quality improvement practices;

• discuss diagnosis and treatment of acute illness in the hospital setting; and

• review current data on diagnostic and therapeutic modalities for common inpatient problems. ■