Sepsis

Sepsis is the clinical syndrome of systemic inflammation, coagulopathy, and often, hypotension produced by the immune response of a person to infection. More than 700,000 cases of severe sepsis occur in the United States each year. In 1991, the Consensus Conference of the American College of Chest Physicians and the Society of Critical Care Medicine put forward a new term to recognize that often the “sepsis syndrome” could occur in persons who suffered insults other than infection. This new term was Systemic Inflammatory Response Syndrome (SIRS) which was defined as the widespread inflammatory response that occurs following a variety of insults such as infection, trauma, pancreatitis, or burns. SIRS is extremely common in hospitalized patients, occurring in over half of patients in a general medical ward and up to 90% in an intensive care unit. Sepsis (infection) occurs in approximately 1 in 5 of all hospital admissions and can progress to severe sepsis with hypotension and poor blood flow to major organs, or eventually, septic shock with hypotension which is (continued on page 2)

It was once said that pneumonia was the old man’s friend. With the advent of antibiotics and high quality supportive therapy, infections can now be treated early in older persons in order to maintain their quality of life. This is often difficult in older persons who have atypical presentations of infections. Infection in an older person may present as a delirium or as a new onset of falls. Many older persons who are infected fail to mount a fever or may have a low, rather than a high, white cell count. Thus, a health care professional needs to have a high awareness of the possibility that an older person has developed an infection in the absence of typical symptoms. (continued on page 6)
not responsive to fluid resuscitation, and organ failure.

Between 1991 and 1997, there was a marked increase in sepsis in hospitalized older Americans (based on Medicare data). This increase has been most prominent in older African American men. Sepsis is now the tenth leading cause of death among older adults in the United States. Over the last decade, there has been not only an increase in the occurrence of sepsis but also an increase in its death rate. Salvie and colleagues in Iowa City studied the factors associated with sepsis mortality in the elderly. Major predictive factors of death included: age, being male, diabetes, hospitalization for cancer, disability of activities of daily living, and cognitive impairment.

While death rates from severe sepsis are highly variable, the overall death rate is approximately a third of affected persons with death rates in young persons being reported to be between 5 to 35% and in older persons 37 to 50%. One year after an episode of severe sepsis, less than one-third of persons are still alive. Recently it has been estimated that sepsis is responsible for $5 to $10 billion of the United States health care budget.

**History of sepsis**

As long ago as 2735 BC, the Chinese Emperor Sheng Nung wrote about the use of herbal medicines to treat fever. Subsequently numerous infections leading to sepsis altered the course of history as was seen in the “Black Death” of the cholera epidemic in Europe, the deaths of the Native Americans when first exposed to Europeans, and the loss of wounded war veterans in the Civil War. The concept of anti-sepsis was first introduced by John Pringle, the Surgeon General of the British army in the 18th century. Nearly a hundred years later, Ignaz Semmelweis introduced antiseptic techniques for the care of women during the birthing process. This reduced the death rate from puerperal fever from 13.6% to 1.5%. In 1879, the French physician Louis Pasteur identified the streptococcus bacteria as the cause of puerperal sepsis. Thirteen years later, Richard Pfeiffer discovered that bacteria released “endo-toxin” in the body of the host resulting in the recognition of a mold as being toxic to bacteless (continued on page 18)
Common sites of infection in older persons

In older persons, infections occur commonly. Because of atypical presentations and in some cases, atypical sites of infection, they are often not diagnosed early. The common sites of infection in older persons are given in the figure below. Several types of these infections are described in this issue of Aging Successfully, with an emphasis on atypical presentations in elderly persons.

**Infective (Bacterial) Endocarditis**

**What is it?**

The endocardium is the innermost of the heart’s three layers and serves as the covering to the interior of the chambers and valves. Normally, the thin, smooth membrane of the endocardium is a hostile environment for infectious organisms, which need a place to lodge and reproduce. If, however, the endocardium becomes roughened or scarred in areas, these sites become potential breeding grounds for bacteria.

In infective endocarditis, a bacterial infection leads to inflammation of the endocardium, particularly the heart valves. Some types of bacteria rapidly cause a severe inflammation of the heart valves. Other bacteria cause a slowly progressive inflammation with fewer symptoms. Infective endocarditis is on the rise among older adults, and doctors predict that it will continue to increase.

**Signs and symptoms**

- Nausea or vomiting
- Loss of appetite
- Disorientation
- Progressive anemia (low hemoglobin count in the blood)
- An unexplained fever
- In some cases, night sweats and chills
- In some cases, the development of a new heart murmur

**Risk factors**

- History of rheumatic fever, as this tends to scar heart valves
- Congenital malformation of the heart or heart valves
- Any type of heart valve disorder
- History of heart valve replacement surgery
- History of any of the following procedures:
  1. dental/oral examinations or procedures that may have caused bleeding;
  2. surgery of the mouth, throat, respiratory tract, and abdominal or genitourinary structures; or
  3. examinations in any of the above areas that may have caused bleeding.

Young and middle-aged adults who contract infective endocarditis are likely to develop a fever, heart murmur, and night sweats and chills. Although some older adults experience the same symptoms, many have less specific complaints such as disorientation, loss of appetite, and nausea. Very often, the major symptoms are lethargy and a general feeling of being unwell.

(continued on page 4)
Sinusitis

What is it?

Sinusitis is an inflammation or swelling of the membrane lining the facial sinuses. It is one of the most common conditions in the United States, affecting close to 32 million people.

Ordinarily, microorganisms and other foreign particles are removed from the sinuses by a layer of mucus, which is constantly propelled by underlying cilia (small “hairs” that beat in a sweeping motion). When this self-cleaning mechanism is impaired, mucus and microorganisms build up in the sinuses, increasing the risk of infection. Sinusitis may be acute or chronic.

Acute episodes of sinusitis may resemble a lingering head cold, with headache, fever, and discolored nasal discharge.

• Chronic cough
• Sore throat
• Unpleasant-smelling breath
• Vomiting on first arising in the morning associated with sudden spasms of coughing
• Sometimes, fever and chills
• Sometimes, headache in forehead; discomfort may grow worse on bending over
• Sometimes, delirium, hallucinations, and cognitive impairment

Risk factors
• Upper respiratory infections
• Allergic rhinitis (“hay fever”); inflammation, due to allergies, of the mucous membrane lining the nose
• Deviated nasal septum
• Overuse of topical decongestants
• Cigarette smoke
• Nasal polyps or tumors
• Swimming and diving
• Dental injections and tooth extractions

Acute episodes of sinusitis may resemble a lingering head cold, with headache, fever, and discolored nasal discharge. Symptoms of chronic sinusitis are more subtle and include a sensation that sinuses are “full,” persistent post-nasal drip, and a chronic cough that occurs in an attempt to clear secretions from the throat.

(continued on page 7)
Saint Louis University Physicians Use New Treatment to Fight Deadly Infections and Severe Sepsis

Study results published in the New England Journal of Medicine offer an addition to antibiotics

Each hour, an average of 20 patients in U.S. hospitals contract sepsis, a serious infection that can lead to multiple organ failure. Sepsis is the leading cause of death in non-coronary intensive care units and the 11th leading cause of death overall. About 750,000 patients develop severe sepsis or septic shock each year and even with the most aggressive current treatments, only about half survive.

It is believed, however, that a new treatment being used by physicians at Saint Louis University School of Medicine is increasing the odds of survival.

Researchers at Saint Louis University School of Medicine and at 163 other sites in 11 countries took part in a study to explore the use of “recombinant human activated protein C” for treatment of severe sepsis in critically ill patients. Recombinant means the protein is genetically engineered using the tools of molecular biology to be a human – not animal – protein. Use of the protein for 96 hours in critically ill patients decreased the mortality rate by up to 20 percent.

“It’s a very important, seminal study because it’s the first trial ever to show there’s something beyond antibiotics that we can use to battle such life-threatening infections, which we’re seeing more frequently,” states George M. Matuschak, M.D., professor of Internal Medicine in the division of pulmonary critical care and occupational medicine and the director of the medical intensive care unit at Saint Louis University Hospital.

To understand how this promising treatment approach works, it is important to understand the body’s response to severe infections. When the infection enters the body, it triggers the inflammatory response and activates the coagulation (blood clotting) process. Although blood clotting is essential for health, inappropriate small “microclots” building up in vessels during sepsis interrupt blood flow to vital organs and deprive the tissues of oxygen. Without oxygen, organ damage occurs and the mortality rate increases.

Physicians use powerful, broad-spectrum antibiotics to fight the initial infection, but antibiotics do nothing to stop the inflammatory and clotting cascades (see pages 12-13) that follow. Researchers discovered, however, that protein C, a naturally occurring protein found in low levels in sepsis victims, reverses the clotting process as well as the excessive inflammation during severe infections.

Given the positive outcomes of protein C-treated patients in this trial, additional studies of recombinant human activated protein C are underway at Saint Louis University Hospital for patients with severe sepsis.
As we begin our journey through the 21st century, infections have made a reemergence as a major cause of disease. This is not only because of the development of new infectious diseases such as AIDS and the Ebola virus, but because of the increasing awareness that many diseases classically not thought to have an infectious cause may have one. Thus, gastrointestinal bleeding due to ulcers in the stomach is now recognized often to be caused by the bacterium, Helicobacter pylori. Ulcers are now cured with antibiotics! There is increasing evidence that atherosclerosis may be initiated by infections caused by Chlamydia pneumoniae. This bacteria can cause inflammation in the endothelial wall resulting in accumulation of cholesterol in the internal layer. It is of interest that the decline in coronary artery deaths began at a time when antibiotic use became widespread before we began to aggressively treat hypertension and hyperlipidemia. A recent study suggests that this organism may also be a trigger for the development of Alzheimer’s disease in some persons.

Older persons are particularly vulnerable to infection because of the changes that occur in the immune system with aging. This is further aggravated when older persons lose weight and develop malnutrition. Not only does malnutrition aggravate the immune system deterioration seen with normal aging, but it also causes a decrease in CD4+ lymphocytes. These changes make the older person particularly vulnerable to infection. The inappropriate use of urinary catheters in older persons represents a common portal for the entry of infectious agents into the person.

As is pointed out in the lead article in this issue, older persons are more prone to develop severe sepsis and more likely to die when they are septic than are younger persons. The recent study showing that the coagulopathy associated with sepsis can be reversed with activated protein-C treatment is particularly exciting to see because this treatment was equally effective in reducing deaths in old as well as young persons with severe sepsis.

Infection was one of the original big five I’s of geriatrics created by Bernard Isaacs in the United Kingdom. It is thus appropriate that this issue of Aging Successfully highlights infections in the older person.

We thank Eli Lilly & Company for an unrestricted educational grant to support publication of this issue.
Common Sites of Infection
(continued from page 4)

Pneumonia

What is it?
Pneumonia is a general term referring to an inflammation of the tissues of the lungs that results from infection. Depending on the cause of the infection and the person’s age and overall health, pneumonia may range from a flu-like annoyance, uncomfortable but temporary, to a life-threatening disease.

Older adults are more likely to develop pneumonia than younger adults. One study revealed an annual hospitalization rate for pneumonia (per 10,000 people) of 30 to 60 cases for those over age 65, compared to 5 to 15 cases for those 65 and younger. Eighty-five percent of influenza and pneumonia deaths occur among older adults. Despite the advances of modern medicine, pneumonia remains the most common cause of death in centenarians.

Signs and Symptoms
- Cough that produces phlegm (sputum)
- Fever
- Sometimes, chills
- Sometimes, intermittent bubbling or crackling noises during inhalation (rales), usually heard through a stethoscope
- Bronchial breath sounds heard through a stethoscope;

these indicate that the lungs have become firm and less elastic (consolidation)
The “classic” symptoms of pneumonia are cough, high fever, and the production of phlegm. These symptoms may be more subtle in older people: the fever may be low or nonexistent, and the cough may seem chronic rather than severe. But the infection may still be serious, even if the symptoms are not.

What causes pneumonia?
Pneumonia can result from a variety of causes: bacteria, vi-
(continued on page 8)
Common Sites of Infection:

Pneumonia (continued from page 7)

ruses, fungi, even chemical irritants. Sometimes, the infectious agent enters the body by being inhaled from the air; for example, in airborne droplets coughed by a person with pneumonia. However, older adults are more likely to contract pneumonia through aspiration (inhaling foreign materials, such as vomit or infected nasal secretions).

A frequent culprit is the bacterium *Streptococcus pneumoniae*, which accounts for 150,000 to 570,000 cases of pneumococcal pneumonia every year. There are more than 85 sub-types of this bacterium, which can cause infections ranging from mildly uncomfortable to life-threatening. Although mild cases may appear to be just a bad cold, more serious strains can lead to dangerous infection and lung congestion.

**Risk factors**

- **Age.** Pneumonia is both more common and more serious in older adults.

- **Influenza ("flu").** Many cases of pneumonia begin with influenza. The hospitalization and death rates for pneumonia show a clear association with the annual “flu season” (winter through early spring in most of the U.S).

- **Institutionalization.** Older adults who are hospitalized or living in nursing homes or long-term care facilities have a much higher risk of contracting influenza and pneumonia. One study found that 750 institutionalized psychiatric patients, all over age 60, had 50 times greater risk of fatal pneumonia than their non-institutionalized peers.

- **Conditions that predispose people to aspirate foreign material, such as vomit.** This includes a wide range of factors, such as sedative use, eating and swallowing disorders, neurological conditions, dementia, alcohol abuse, seizures, and anesthesia.

- **Chronic obstructive pulmonary disease (COPD) and other chronic lung conditions.** People with these conditions show higher rates of pneumonia and seem to fare less well when pneumonia develops. One reason may be that they are less able to “cough up” infected secretions.

**How is it diagnosed?**

Tests that are useful for diagnosing pneumonia include the complete blood count (CBC), chest X-rays, and an examination of respiratory secretions through a microscope. If the CBC shows an unusual number of white blood cells, this indicates an infection; however, white cell levels may not be as high in older adults with pneumonia as they are in younger adults. Although a chest X-ray may be normal early in the disease, generally it will reveal an area of fluid build-up in the lungs. Microscopic examination of respiratory secretions can help with the identification of the specific cause of the infection.

Some older adults may have fairly mild symptoms, even though chest X-rays show areas of congestion in one or both lungs (“walking pneumonia” or “nursing home pneumonia.” Generally these are cases of bacterial pneumonia (often caused by unusual organisms such as *Mycoplasma, Legionella, or Chlamydia*) which respond to antibiotics. Tuberculosis may also present as a pneumonia in the upper lobes of the lung in older persons. It is especially common in those with diabetes.

**How serious is it?**

Before the introduction of antibiotics, 70 percent of people in their 70s who developed pneumonia died from it. Today, the picture is much brighter; the mortality rate has fallen significantly. However, pneumonia remains a serious health challenge, and it is important to seek prompt medical treatment.

(continued on page 10)
Like it or not, the world is going gray. Europe and North America have a higher percentage of aged citizens than do other regions in the world. Sweden and Greece, for example, are the world’s oldest countries with 17.2% of their populations aged 65 and older. In Poland, with the youngest European population, that percentage is 12.2 and in the United States it is 12.7. Other areas of the world have smaller estimated percentages of 65+ citizens: 10% in Oceania, 5% in Latin America, Asia, and the Caribbean, 4% in the Near East and North Africa, and 3% in Sub-Saharan Africa. For those who are interested in the demographics of specific countries, the Census Bureau website is an excellent resource (www.census.gov/cgi-bin/ipc/) that provides population pyramids of individual countries.

In Europe and North America, it has taken 50-100 years for the 65 and older population to double from an average of 7 to 14%. In other countries, where the percentages of the 65+ population are significantly less, the doubling of that older population has taken only 30 years. Two primary reasons are responsible for this aging of the world’s population: falling fertility rates and rising longevity rates. The falling fertility rate results in a decreased number of young persons while the rising longevity rate results in an increased number of old persons.

As the US population has grown older, the federal government has provided funding for the development of 45 Geriatric Education Centers (GECs) which have been responsible for developing educational programs to train health care providers about the unique medical needs of the elderly. Just recently, the faculty of these GECs have begun to create outreach programs to assist faculty in other countries with the development of similar training programs there. The Gateway GEC faculty are participating in this program.

Examples of Gateway GEC faculty activities in international aging include the following: Drs. William A. Banks and John E. Morley presented papers at the “Anorexia During Disease – From Research to Clinical Practice” conference in Ascona, Switzerland in October 2000. Anorexia, which literally means “no appetite” is a common affliction of the elderly and can lead to severe weight loss, malnutrition, muscle weakness, frailty, and other complications. Dr. Banks spoke about his research on how cytokines affect the brain to produce anorexia, and Dr. Morley spoke about his research on how anorexia affects the elderly and ways to do something about it. Ascona is located in a Swiss canton famous for its Italian cuisine. Neither Dr. Morley nor Dr. Banks suffered from anorexia while attending the conference.

While in Europe, Dr. Banks also presented his work to scientists at Cambridge University in England on how the AIDS virus crosses the blood-brain barrier. Dr. Banks also spoke recently on his research related to stroke and a substance called PACAP at Showa, Waseda and Nagasaki Universities in Japan.

In the last few months, Dr. Morley has been invited to speak in Asia (Japan, China, Hong Kong, and Vietnam) as well as Europe, Canada, and Australia on the Andropause. The Saint Louis University ADAM questionnaire has been translated into Chinese and a number of European languages. Dr. Morley has provided advice to the Mexican Social Security System and also to Dr. Joel Rodriguez-Saldana who has conducted a ten-year longitudinal study on aging in Mexico City. He has advised Dr. Ian (continued on page 22)
Common Sites of Infection
(continued from page 8)

Urinary Tract Infections

What is it?

Bacteriuria (the presence of bacteria in the urine) is a condition that becomes more common with age. Before age 65, less than 5 percent of women and 1 percent of men have bacteriuria; after 65, the condition exists in at least 20 percent of women and 10 percent of men. Bacteriuria does not necessarily indicate that a urinary tract infection is present. The urine of many healthy people contains bacteria from time to time, and people who harbor bacteria do not always have symptoms of urinary tract infection. In fact, researchers believe that most older women experience episodes of bacteriuria without any symptoms.

Sometimes, however, bacteriuria does become serious enough to cause a urinary tract infection. It is estimated that as many as 10 percent of older adults experience a bacterial infection of the urinary tract each year. Many people experience recurring infections; some women have recurring infections after sexual intercourse. The organism most often responsible for causing urinary tract infections is Escherichia coli, a normal inhabitant of the intestines.

The most common type of infection is cystitis, an inflammation of the wall of the bladder that may involve the urethra. In 8 to 10 percent of cases, the infection is pyelonephritis (inflammation of a kidney, usually caused by a bacterial infection).

Signs and symptoms

- Pain or burning sensation during urination
- Difficult urination
- Frequent urge to urinate
- Sometimes, urine contains blood or is foul-smelling
- Sometimes, fever and chills
- Sometimes, back pain
- Sometimes, urinary incontinence

Risk factors

Any health condition that allows urine to pool in the bladder can increase risk of developing a urinary tract infection. Specific risk factors include:

- An in-dwelling urinary catheter. One study of nursing-home residents found that those with in-dwelling catheters were almost 40 times more likely to develop serious urinary tract infections.
- Recent cystoscopy procedure
- Poorly controlled diabetes. When diabetes is not well controlled, the level of glucose in the urine rises, creating a more favorable environment for the growth of bacteria.
- Urinary tract obstructions that block the free flow of urine. If urine is not completely excreted, bacteria may multiply in the residue.
- In men, an enlarged prostate gland or prostate cancer
- In women, relaxation of the pelvic floor muscles that occurs after multiple births. This may allow the bladder to drop, creating a residual pool of urine after voiding.
- History of urinary tract infections. Infections may recur if the underlying cause is not treated.

People with a history of one type of infection, such as cystitis, have a greater risk of developing other types, such as pyelonephritis.

(continued on page 11)
Common Sites of Infection
(continued from page 10)

Diverticulitis

Diverticulitis is the inflammation of a diverticulum, a small pocket in the wall of the colon that has filled with stagnant fecal matter and has become inflamed.

Signs and Symptoms

• Colicky pain (spasmodic pain that occurs in waves) in the lower left abdomen
• Pain grows worse after meals and improves after bowel movements or passing gas
• Changes in bowel habits (usually constipation or alternative bouts of constipation and diarrhea)
• Blood in stool
• Sometimes, tenderness in the lower left abdomen
• Sometimes, fever

Diagnosis

Doctors may be able to diagnose diverticulitis based on symptoms. These symptoms may be less pronounced in older adults than in younger people – for instance, older adults may not have a high fever or extreme abdominal tenderness. A barium enema and X-ray can reveal the outward projections of diverticula from the colon wall; or the diverticula may be seen during colonoscopy or on a CT scan. Deciding whether or not these diverticula are infected, however, can be extremely difficult.

Diverticulitis-like symptoms can be caused by several other conditions, especially appendicitis, colon tumors, or inflammatory bowel disease. A flexible sigmoidoscopy (visual examination of the lower [sigmoid] colon) or a full colonoscopy can rule out these possibilities.

Treatment

Mild cases of diverticulitis often respond to a liquid diet along with antibiotic medications to quell any infection. If the diverticulitis is serious, surgery may be necessary to bypass or remove affected portions of the colon. If perforation and peritonitis occur, this is an emergency; immediate surgery is needed to remove perforated tissue.
The Sepsis Cascade: An interaction of Inflammation

- Injury
- Bacteria
- Fungus
- Virus
- Parasite

Cytokine Release
- TNFα*
- Interleukin-1
- Interleukin-6

- Tissue Factor
- Factor VIIIa
- Factor V
- Inhibition of Thrombomodulin
- Elastase
- Decreased Antithrombin III

* Tumor necrosis factor α.
† Thrombin-activatable fibrinolysis inhibitor
‡ Plasminogen activator inhibitor-1

Questions? FAX: (314) 771-8575 • email: agingsuccess@slu.edu
Decreased organ perfusion

Organ dysfunction

Vasodilation

Hypotension

Shock

Decreased organ perfusion

Death

Fever

Anorexia

Cachexia (muscle protein loss)

Nitric oxide release

Endothelial injury

COAGULOPATHY

D-dimer

thrombin

Suppressed fibrinolysis

PAI-1

TAFI

PAI-1

Decreased protein C

Microvascular thrombosis

Fibrin

Questions? FAX: (314) 771-8575 • email: agingsuccess@slu.edu
Geriatrics Continues to Play

We first introduced readers to our use of games to teach geriatrics in the Winter 1998 (Vol. VIII, No. 1) issue of Aging Successfully. That article summarized reasons for using games to improve understanding and knowledge about aging and talked about which types of games work best for which groups of learners. Since that time the faculty of the Gateway Geriatric Education Center (Gateway GEC) has continued to practice what it preaches, both by using the games that were reviewed 3 years ago and by creating new, or improving existing, aging games. As a result, it is time for an update on new and improved aging games designed to increase our understanding of aging.

Senior Safety Solitaire, which promotes both home and personal safety, was first introduced by the GEC three years ago. The first edition has sold out and, based on the feedback of the original users, a second edition, the Multicultural Edition, is now available. This game is one of the most versatile games on aging available today. It is designed to provide safety information for older adults, volunteers, para-professionals, and professionals alike. It can be played by a single player or by a group. Several agencies have reported back that the game has been used successfully at health screenings as well as in nursing homes, community centers, apartment buildings, and assisted care settings. Others have used it successfully with nurses, physicians, students, therapists, social workers and geriatric care managers. Because the program was developed for urban settings, it has been used less frequently with elderly dwellers of private homes but several facilitators report that with a few modifications in expectations about the existence of such things as street lighting, elevators, and sidewalks, it can be easily adapted to more suburban and/or rural settings. Probably the most unexpected use of the game was by a group of concerned parents to train college-aged students what safety issues to be conscious of when choosing off-campus housing.

Geropady, a highly competitive game created by John E. Morley over a decade ago, continues to be a popular game, especially with medical students. Dr. Roger Wong of Vancouver General Hospital and the University of British Columbia, Canada, has adapted the game to the computer. Regular readers of Aging Successfully are well aware of the Crossword Puzzles that are now published in each issue. These puzzles were originally introduced for the reader who preferred a more solitary pursuit of education. However, Dr. Margaret Wilson, the Division of Geriatric Medicine's newest faculty member, has found a creative way to use the puzzles to teach medical students. She has distributed 5 puzzles to teams of medical students and has given prizes to teams with the most correct answers, the most innovative answers, and the fastest turnaround. This will work as long as the students do not realize that the puzzles (and their answers) can be found in our newly published anthology of puzzles, the Geriatric Crossword Puzzle Book. The book currently contains 23 puzzles and is designed to make the addition of newly created puzzles easy.

The GEC faculty has entered the 21st century with the latest in teaching methods. The latest game to be produced by the Gateway GEC faculty is Longevity, a web-based, interactive educational game. To play, visit www.HealthandAge.com and look for Longevity under GAMA (Global Academy for Medicine in Aging). The game has over 200 questions distributed over eight levels and allows you to test your knowledge of geriatrics diagnostics and management as you help your patients move from ICU to assisted living. You can play for your own edification or you can compare yourself against previous players. Highest scorers receive the

(continued on page 22)
The MOGGEC Injury Prevention Project presents this multi-cultural game, Senior Safety Solitaire, that promotes both home and personal safety. This game comes complete with pictures of safety problems and solution cards and is designed to provide safety information for older adults, volunteers, para-professionals, and professionals, and can be played by a single player or by a group. Price: $65.

**To order:**
Please send check or money order to:
SLU-HSC
Senior Safety Solitaire
Division of Geriatric Medicine
1402 S. Grand, Room M238
St. Louis, MO 63104
For more information, please call 314-577-8462.

**Sepsis Puzzle Answer (From page 14)**

**Can’t get enough? Want more?**
The entire collection of our crossword puzzles is now available. A book containing 23 puzzles on various medical, psychiatric, and social topics has been published by the Division of Geriatric Medicine. The books are available for $16.50. To order, send check or money order to: Saint Louis University Division of Geriatric Medicine, Attn: Ronna Rhodes, 1402 S. Grand, Rm M238, St. Louis, MO 63104

**Topic: Mental Health/Treatment**
An 82 year old presents with a 50 pound weight loss, atrial fibrillation and proximal muscle weakness. His eyes are hooded. He is depressed. He has a history of smoking two packs per day and has COPD. A cortisol level is 27 mg/dl. Which of the following tests would be most helpful in making the diagnosis?

A. Birmingham Apnea Score
B. Epworth Sleepiness Apnea Score
C. Polysomnography
D. London Sleep Score
E. Presence of obesity

**Current High Scores**

- Tracy: 10,000
- Smith: 9,775
- David: 7,850

**Score:** 23400
**Level:** 8
**Question:** 10/10
University of the Third Age Update

Dr. Nina Tumosa attended the 20th International Congress of the Association Internationale for the University of the Third Age (AIUTA) in Quebec City, Canada in the fall of 2000. Representatives from 19 countries attended the three-day conference which addressed the use of the internet and computers by seniors to continue their education and to promote cultural understanding. AIUTA is the international administrative arm of the University of the Third Age (U3A). Individual chapters of the U3A are found throughout the world. The first chapter began at the University of Toulouse in France in 1973. Since then, chapters have opened in almost every country in Europe as well as in such places as Australia, Brazil, Canada, Chile, China, Japan, and New Zealand, with the newest chapters in Senegal, Slovakia, and the United States.

The mission of U3A chapters is to provide opportunities for retired individuals (“Third Agers”) to continue their intellectual, social, cultural, spiritual, and physical development in association with others in a stimulating environment. Goals of the local St. Louis chapter include assuming responsibilities as citizens of the community and the world, tapping the potential, energy, and creativity of “Third Agers”, and participating in studies and research relating to aging.

The local U3A chapter has several on-going programs that are open to interested persons. These include a monthly book discussion group, a weekly memoir-writing group, and two day-long conferences (one each in the spring and fall) that feature a keynote speaker, followed by several workshops that cover such topics as local history, exercise, health, personal finances, and spirituality. To obtain further information about the U3A, contact Ronna Rhodes at Saint Louis University, Division of Geriatric Medicine, 1402 S. Grand Blvd., Room M238, St. Louis, MO 63104.

While at the Quebec meeting, Dr. Tumosa was elected to the board of the AIUTA, the first American to be so honored. As part of her duties to the board, she will work with AIUTA to promote the development of other American U3A chapters, an American program on the development of an internet-available databank containing memoirs of World War II veterans, and an international program devoted to the preservation of cultural diversity which will collect language dictionaries, photo albums, cookbooks, and other such documents that will promote international understanding through common cultural instruments. Examples of the latter project will be presented by Third Agers from around the world at the next international meeting in Geneva, Switzerland on October 3-5, 2002.

Upcoming CME Programs

The 12th Annual Saint Louis University Symposium for Medical Directors in Nursing Homes and the 21st Annual GRECC Symposium December 7, 8, 2001

Reunion Weekend: Geriatrics Review October 12, 2001

University of the Third Age Conference October 27, 2001

All the above conferences will be held at Saint Louis University. For more information, please call 314-577-8462.
Sepsis

ria, ushering in the era of antibiotics to treat bacterial infections. Toward the end of the twentieth century, it became clear that sepsis results in the release of a host of inflammatory mediators such as tumor necrosis factor-a and interleukin-1 which result in the production of nitric oxide (leading to hypotension), as well as other mediators producing capillary injury, and eventually, organ dysfunction. This damage to the endothelium leads to activation of the coagulation cascade with the production of thrombin. This coagulopathy leads to microvascular thrombosis and multi-organ failure. It also results in consumption of endogenous regulators of thrombolysis such as protein-C and Antithrombin III. This results in continued endothelial damage, organ ischemia and damage, and ultimately, death in many patients (see pages 12-13).

Clinical features

The hallmark clinical manifestations of SIRS are two or more of the following conditions:

- Temperature > 38ºC or < 36ºC
- Tachycardia > 90 beats per minute
- Respiratory rate > 20 per minute or a PaCO₂ < 32 mm Hg
- White blood cell count > 12,000 mm³ or < 4,000/mm³ or > 10% immature (band) forms (“left shift”)

The other symptoms and signs associated with sepsis include the signs of peripheral vasodilation and hypotension and altered mental status. Mental status changes include lack of attention, decreased orientation, confusion, agitation, lethargy, and eventually coma. Prior to the development of hypotension, patients with sepsis may have a high output cardiac state with a wide pulse pressure associated with a tachycardia. Prolonged sepsis is associated with neuromuscular weakness, the so-called critical illness, polymyopathy. Severe muscle wasting (cachexia) is associated with sepsis. Cytokines result in a catabolic response from muscle with the breakdown of myofibrillar proteins and the release of amino acids into the circulation. Clinically, besides muscle wasting and weakness which slows ambulation and rehabilitation, it can also result in respiratory muscle weakness with delayed weaning from the ventilator and an increased propensity to develop pneumonia.

Gastrointestinal manifestations of sepsis include jaundice, gastrointestinal bleeding, and slowed gastrointestinal motility. Decreased urine output and, eventually, renal failure are not rare in persons with severe sepsis. Both hyper- and hypoglycemia may occur, as well as lactic acidosis and electrolyte abnormalities.

The reduced levels of protein-C and antithrombin III, as well as a marked decline in platelet numbers, lead to the coagulopathy which can present with organ pain secondary to ischemia, gangrene of the digits, purpura, and bleeding from multiple sites.

Older persons often tend to have atypical responses to sepsis... particularly by presenting with delirium early.

Sepsis-Related Definitions

“Severe sepsis” is sepsis associated with organ dysfunction, hypoperfusion, or hypotension (systolic blood pressure < 90 mmHg or a reduction of > 40 mm Hg from baseline).

“Septic shock” is a subset of severe sepsis with SIRS induced hypotension despite adequate fluid resuscitation and may include lactic acidosis, oliguria or altered mental status.

“Multiple Organ Dysfunction Syndrome (MODS)” occurs when multiple organ systems fail.

Older persons often tend to have atypical responses to sepsis. This includes the failure to mount a fever and even presenting early on with hypothermia. Thus the classical chills and sweating of sepsis are often absent. Leukopenia is common as well. The older person may only have a left shift. In particular, older persons are much more likely to present with delirium early during sepsis. This delirium may take the form of lack of attention or non-responsiveness. Thus, for example, a demented patient who screams frequently may stop screaming. New onset of falls in an older person may be the only evidence of a sepsis-associated delirium. The peripheral vasodilation of sepsis can result in an older person presenting with syncope. Older persons classically have (continued on page 20)
Guide to Cough Symptoms

Note: This information is not intended to replace the services of your health care provider. Always consult your provider immediately if you are concerned about your cough and follow his or her instructions.

Cough
What is it?
A noisy expulsion of air from the lungs. Coughing is one of the protective mechanisms the body uses to rid itself of substances within the respiratory system. A cough may be “productive” (that is, it produces sputum [phlegm]) or “dry.”

Do you have a postnasal drip (irritation at the back of your throat), early morning vomiting, and/or sinus pain?

Yes

You may have sinusitis, an inflammation of the paranasal sinuses. Steam inhalation, nasal decongestants, and analgesics may relieve your symptoms. If not, discuss the problem with your doctor.

No

A dry (nonproductive) cough may be an early sign of heart failure or a side effect of taking an ACE inhibitor, a type of medication that is often prescribed for heart failure.

Yes

Is your cough productive (that is, does it produce phlegm)?

No

Is the cough constant or nearly so?

Yes

You may have chronic bronchitis, an inflammation of the mucous membranes lining the airways of the lungs. Consult your doctor.

No

Does the phlegm have a yellow tinge?

Yes

Several respiratory conditions, including pneumonia and acute bronchitis, an inflammation of the mucous membranes lining the airways of the lungs, are characterized by an acute, productive cough. Consult your doctor.

No

Is the phlegm blood-tinged?

Yes

Your symptoms require evaluation. Consult a doctor without delay! If you also have a fever, you may have pneumonia. If your symptoms developed suddenly and you are experiencing pain and difficulty breathing, you may have a pulmonary embolism. Lung cancer may also cause symptoms of a constant, productive cough and blood-tinged sputum; you are at risk for lung cancer if you have smoked for many years.

If you are unable to diagnose your symptoms using this chart and your cough persists for more than 4 days or worsens, consult your doctor without delay!
Sepsis

less tissue reserve which makes them more vulnerable to stressors. Thus organ dysfunction such as renal, respiratory, or cardiac failure may present earlier in the course of sepsis. Older persons are also more likely to develop septic shock and multiple organ dysfunction syndrome (MODS). In addition, older persons more commonly have genitourinary, gut, or respiratory sites of infection, making it more likely that they have sepsis on the basis of a gram-negative bacillus. Finally, older persons can show markedly prolonged rehabilitation times from severe sepsis, and sepsis may be the event that precipitates their entry into a nursing home.

Factors contributing to the development of sepsis

The reasons for the increased occurrence of sepsis and septic shock are uncertain but the increase in the number of risk factors for sepsis may play a major role. As we all recognize, the population is aging and older persons have a variety of changes in their immune system that make them at increased risk for developing infections. This is particularly true in older persons with multiple diseases. Older persons are particularly prone to develop weight loss and malnutrition. This leads to a further decline in their immune system and a decrease in CD4+ lymphocytes. The decline in the CD4+ to CD8+ ratio results in an inability to mount an adequate host response to infections. This results in unusual infections as is seen in patients with acquired immunodeficiency syndrome (AIDS). Sakkinen and colleagues, in examining a subgroup of the Cardiovascular Health Study, all of whom were over 65 years of age, found that older women had lower protein-C levels. This would put older women at particular risk for developing severe coagulopathies during sepsis.

Diseases specifically increasing the risk of sepsis include diabetes mellitus, malignancy and AIDS. Diabetes occurs in almost 1 in 5 older persons. Half of the persons with diabetes are over age 60. Alcoholics are also at increased risk of sepsis. Persons who acquire a second nosocomial infection are at increased risk of death from sepsis.

Iatrogenic factors may be particularly responsible for the increase in sepsis in older persons.

Iatrogenic factors may be particularly responsible for the increase in sepsis in older persons. Urinary catheters are associated with more than one febrile episode every hundred patient days. These episodes are associated with a highly significant death rate in older persons. Insertion of intravenous catheters, particularly in the jugular, leads to an increased risk of sepsis death. Because it is often difficult to maintain peripheral venous access in older persons, they are at increased risk of receiving central venous catheters. Because of their multiple diseases and atypical presentations, older persons are also at increased risk of having other invasive procedures that put them at risk of sepsis. Older persons often receive antibiotics because of recurrent infections and so they are more likely to develop resistant microorganisms. The use of cytotoxic and immunosuppressive agents to treat malignancies and autoimmune disorders further increases the chances of a person developing sepsis. Infections often occur in unusual places in older persons leading to the diagnosis being missed early in the disease process.

Treatment

The primary treatment in a person with sepsis is appropriate antibiotics. This requires identification of the organism as early as possible. Appropriate antibiotic therapy has been shown to halve the subsequent mortality, as has empirical antibiotic therapy. Anti-microbial therapy in patients with fungal septicemia also appears to reduce the mortality rate.

Dennis Sullivan at the University of Arkansas has pointed out that we tend to starve older persons while they are in the hospital. Persons with sepsis should get 25 to 30 kcal/kg daily with 1.5 to 2.0 g/kg coming from protein. In general, enteral nutrition is preferred to parenteral nutrition because of its reduction in stress ulcers, costs, and gut protection. It is possible that immunomodulatory formulas may be preferred over regular formulas.

In an attempt to attenuate the ongoing inflammatory cascade of sepsis, numerous agents have been tested. Two meta-analyses failed to find any value in utilizing corticosteroids during sepsis and suggested they may even be harmful. There is no evidence to support other anti-inflammatory agents such as ibuprofen,

(continued on page 23)
PEPTIDES, Elsevier Science Inc., and the Department of Psychology, University of New Orleans, are proud to announce that

John E. Morley, M.B., B.Ch.,
Director, Division of Geriatric Medicine
Saint Louis University School of Medicine
and Director, GRECC, St. Louis Veterans Affairs Medical Center
Has been selected as the 2001 winner of the Gayle A. Olson and Richard D. Olson Prize.

The citation for the winning article is

Dr. Morley visited the University of New Orleans, received the prize, and presented his address

“Alzheimer’s Disease through the Eye of a Mouse”
on April 24, 2001.

The Gayle A. Olson & Richard D. Olson Prize is awarded annually to the senior author of the most meritorious original research article on the behavioral effects of peptides published during the previous year in PEPTIDES. The Olson Prize was inaugurated in April 2001, on the occasion of the Olsons’ retirement from the Department of Psychology at the University of New Orleans, to honor the outstanding contributions of Dr. Gayle A. Olson, Research Professor, and Dr. Richard D. Olson, Research Professor, to the field of peptide research over the past three decades. All behavioral articles published in PEPTIDES during the calendar year are automatically considered for the Olson Prize. The recipient receives a Certificate of Award, a cash prize of $2,500, and a trip to The University of New Orleans to deliver the keynote address describing the research for which the Olson Prize was given at the annual Gayle A. Olson & Richard D. Olson Prize Seminar.
The Old Beauty

By Bahar Bastani, MD
April 15, 2001

I walked into her room quite hurriedly
In a rush to finish rounds very rapidly
I saw an old black woman, calm, in her bed
Helpless, pleasantly demented, lying in bed
The food tray at the bedside was not touched
The applesauce, soup, and the broth were untouched
Her thirsty lips and dry mouth showed a great desire
For a sip of soup or water, if they could acquire
My rush to finish rounds and go to my office
Was halted when our smiles exchanged a kiss
The food tray would have been taken away very soon
By the harried nurses, darting in and out of her room
One had to slow down to see the beauty of 92 winters
In her old face, covered with so many deep wrinkles

I slowed down and helped her to take small sips
Of her soup and broth, followed by water sips
She thanked me with a smile on her face
I thanked her, allowing me to help in her case
I had looked through her eyes into the eyes of God
I had seen on her face the smile of God
I had touched through her heart the heart of God
I had fed through her lips the mouth of God
I asked, “Why had God left those who needed help?”
He smiled, “Didn’t I make those who could help?”
“My hands, eyes, and ears are those who care
My love and help flows through those who care”
“I am the Helper, the Needy, and the Help itself
I am the Lover, the Beloved, and the Love itself”
pentoxifylline, or prostaglandin E1. Oxygen scavengers, interferon \(\gamma\), TNF\(\alpha\), and growth hormone have not been shown to be useful in the management of sepsis. Antithrombin III, an inhibitor of a number of coagulation factors, showed promise in treating sepsis in some placebo-controlled small trials, but a large, multi-center, prospective, double-blind study failed to demonstrate a significant improvement in survival.

A recent large double-blind randomized trial (the Protein C Worldwide Evaluation in Severe Sepsis [PROWESS], the abstract of which may be viewed at www.nejm.org [March 8]) examined the effect of recombinant human activated protein-C (drotrecogin alfa) in 1690 patients. This drug appears to be able to reverse the cascade of inflammation, coagulation, and fibrinolysis that occurs with sepsis. The average age of the patients was 60.5 years with approximately a quarter being over 75 years of age and 56% over 60 years of age. By 28 days, 30.8% of the placebo group died, compared to 24.7% of the drotrecogin alfa group. The absolute reduction in the risk of death was 6.1%. Overall, serious adverse side effects were equal in both groups, though, as might be expected, there was an increase in bleeding episodes in the drotrecogin alfa group. Drotrecogin alfa reduced levels of interleukin-6, a marker of inflammation, and of D-dimer, a marker of coagulopathy. Outcomes were similar in persons over 60 years of age compared to those under 60 years of age.

**Conclusion**

Sepsis remains a condition with extremely high fatality rates in older persons. Early recognition of infection and treatment with empiric antibiotics remains the cornerstone of appropriate treatment. Adequate nutrition support needs to be given to all patients. A recent study utilizing activated protein-C has shown that mortality can be further decreased by using this compound in persons with severe sepsis.
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