GERONTOLOGICAL CONSIDERATIONS

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Many infections have more severe manifestations in older adults. This increased severity has been attributed to comorbid conditions, waning immunity, suboptimal nutritional status, and social and environmental factors. Residence in long-term care facilities may be a strong factor in exposure to normal and drug-resistant pathogens.[56] Pneumonia is a common and sometimes fatal infection, whether acquired in the community or in healthcare facilities. With the reduction in adaptive immunity associated with aging, there is sometimes reemergence of latent viruses. Finally, HIV can be acquired and has a somewhat different presentation in adults older than 50 years of age. These examples are described further in this section.

COMMUNITY-ACQUIRED PNEUMONIA

Pneumonia can be classified as either community-acquired pneumonia (CAP) or healthcare-acquired pneumonia (HCAP). HCAP is defined as infection in an individual whose symptoms began after more than 2 days of a hospital stay or 10 to 14 days after being discharged.[57] Distinguishing between the two is key to proper treatment, as the microorganisms accountable for the two types are vastly different.

Recent data show that CAP is the third most common hospitalization diagnosis in adults 65 years of age or older and the leading cause of septic shock. Current guidelines recommend that adults aged 65 years and older receive both the pneumococcal (one dose of the 23-valent vaccine) and the influenza (annual) vaccines.[58] In comparison with the younger population, CAP in the elderly patient carries an increased risk of morbidity and mortality. Because an impaired immune response and other physiological changes that occur with aging create increased vulnerability in this population, fast diagnosis and treatment, and hemodynamic stability, are important when dealing with these patients. Exogenous factors such as frailty, comorbidities, mechanical swallowing disorders, and sedentary lifestyle all contribute to the increased risk of mortality and need for ICU admissions.

Clinical manifestations of CAP in elderly patients differ from findings in younger adults. A subtler presentation may occur; therefore, the absence of typical symptoms such as cough, fever, or elevated white cell count cannot rule out a diagnosis. Additionally, atypical presentations such as altered mental status, frequent falls, anorexia, incontinence, or an overall decline in function may be the only presenting manifestations of the diagnosis in the elder adult.

Diagnosis depends on chest x-ray evidence of opacities. There is much debate over the usefulness of laboratory testing as biomarkers for the diagnosis of CAP in the geriatric patient. Tests such as white blood cell count, C-reactive protein, and procalcitonin are widely used in today's medical practice, but insufficient data over the years have yet to truly prove their sensitivities.[57,58] Age-related alterations in the immune system can create false laboratory results, especially in tests involving inflammatory responses. Other tests that can be useful in supporting a diagnosis are blood cultures, Gram stains, respiratory sputum cultures, and checking the patient's urine for the presence of pneumococcal and *Legionella* antigens. However, in over half of patients, the causative organism cannot be identified.

The most common cause of CAP in older adults is *S. pneumoniae*, followed by *Haemophilus influenzae*. Compared with younger adults, the frequency of atypical strains of pneumonia caused by *Legionella*, *Mycoplasma*, and *Chlamydophila* organisms is lower in the elderly patient.[58] *S. pneumoniae* is part of the normal oral and upper respiratory flora and can enter the lower respiratory passages by inhalation and by aspiration, with the latter being the most common route in older adults. Pneumococcal capsular antigens protect the bacteria from phagocytosis and define serotypes, and several of the antigens are the targets of pneumococcal vaccines. Additional pneumococcal virulence elements include pneumolysin, a pore-forming toxin that promotes host cell damage and death and exacerbates inflammation. Bacterial proteases are able to cleave and inactivate host IgA as well as the mucus protective barrier, disabling mucociliary clearance. Other surface and secreted proteins block complement binding and degrade complement proteins. Respiratory compromise in pneumonia is due to the inflammatory response that promotes fluid entry into alveoli, limiting gas exchange. This is exacerbated when viral and bacterial coinfection occur, synergizing to enhance inflammatory responses.[59]

In addition to acute inflammation and risk of sepsis, pneumonia in older adults is associated with cardiovascular morbidity and mortality. Rates of myocardial infarction and ischemic stroke increase during and after an episode of pneumonia, and this is attributed to hypercoagulability associated with the inflammatory state and bacteremia.[60] In addition, older adults with other comorbidities, including heart failure, atrial fibrillation, and chronic obstructive pulmonary disease, have higher morbidity and mortality rates secondary to pneumonia.[61]

Two important prognostic scales widely used to predict 30-day mortality risk for a patient with CAP are the Pneumonia Severity Index (PSI) and CURB-65. The PSI assigns points for various categories, including both laboratory results and clinical symptoms. Once the points have been tallied, patients are placed into one of five risk categories, increasing in severity, to determine who should be hospitalized. CURB-65 uses a formula based on five markers: (a) confusion, (b) urea level >7 mmol/L, (c) respiratory rate of 30 breaths/min or more, (d) systolic blood pressure <90 mm Hg or diastolic blood pressure ≤60 mm Hg, and (e) patient age of 65 years or older. Studies have shown that one of the biggest flaws in the CURB-65 model is that it does not take into account oxygen saturation or the functional status of the patient. These formulas are intended to supplement the practitioner's diagnosis and help in risk stratification to achieve better long-term outcomes.[57,58]

VARICELLA-ZOSTER VIRUS

Varicella-zoster virus (VZV) is a member of the Herpesviridae family consisting of enveloped, double-stranded DNA-type viruses. As such, the viral DNA is able to reside in the host cell nucleus, forming a latent infection that can be reactivated months and years after the initial exposure. VZV in children causes chickenpox, a highly contagious disease with respiratory transmission and cutaneous lesions that may also spread the infection. Latent infection affects sensory neurons in dorsal root ganglia and cranial nerve ganglia. With aging, as immune protection against VZV wanes, reactivation causes **shingles**—the unilateral painful sensory neuropathy and skin blistering associated with a particular facial or spinal segment (dermatomal distribution). Severe cases may be followed by **postherpetic neuralgia**, a chronic pain syndrome that may last from months to years. Vaccination for VZV is strongly recommended for individuals aged 60 years and older, as the risk of shingles increases with age.[62,63]

HIV

In 2017, 17% of HIV diagnoses were made in people 50 years of age and older. In 2016, Americans aged 55 and older accounted for almost 30% of the population living with HIV infection.[64] Although risk factors for contracting HIV infection remain the same for adults of all ages, the elderly are often less aware of these factors. For this reason, and because of the effects of immunosenescence, diagnosis of HIV in the elderly may occur later in the disease course, often with higher rates of morbidity and mortality and comorbid disease complications. The persistence of immune activation and continued inflammation associated with HIV, combined with the natural effects of aging on the immune system, result in profound havoc; thus, age may be considered to be an independent predictor of clinical progression of HIV.[65,66]

The stages of HIV infection in older adults do not differ from those outlined earlier in the chapter, but as a result of advanced age, these patients may have greater loss of CD4 cells, as well as lower counts of total and functioning CD8 cells, which are crucial for limiting the replication of the HIV. Furthermore, the progression of HIV may be more pronounced in the elderly because the infection itself can inhibit the generation of naive T cells. The net result is greater severity of HIV infection and the potential of more rapid transition to AIDS in older adults, as has been noted for several infections in this population.

CASE STUDY 5.1: A Patient With Acute HIV Infection

Sampath Wijesinghe

Patient Compliant: *"I just got back from a mission trip to Haiti and have been having fevers, sore throat, body aches, and headache for the past 5 days. I thought I'd be feeling better by now, but I don't think I'm improving. I'm wondering if I could have malaria. I didn't have a chance to get this year's flu shot or malaria prophylaxis before my trip."*

History of Present Illness/Review of Systems: A 19-year-old Hispanic man presents to his primary care provider at the university health center during the winter quarter with a 5-day history of fever, sore throat, body aches, and headache. About 4 weeks ago, he went on a mission trip to Haiti. While in Haiti, he had unprotected sex with a female student who was also participating in the trip as well as a male Haitian student. He is concerned about his symptoms as they are not resolving and is requesting an evaluation of his condition. He has been resting and drinking plenty of fluids for the last 5 days, and has also been taking acetaminophen, 500 mg, every 4 hours, as needed for his fever. The fever has decreased slightly and he thinks the acetaminophen has helped with the body ache, sore throat, and headache. The review of systems is positive for fever, fatigue, and anxiousness. The patient reports having headache, sore throat, and myalgia. The review of systems is negative for cough, nausea, vomiting, diarrhea, constipation, abdominal pain, rash, ear pain, dysuria, urinary urgency, back pain, chest pain, and shortness of breath.

Past Medical/Social/Family History: The patient's past medical history is significant for appendectomy (at age 9) and chlamydial infection (at age 17). An HIV test performed at the time of the chlamydia diagnosis was negative. Social history includes drinking a six pack of beer each weekend (Friday and Saturday nights) since age 18 and having three different girlfriends over the last year. He has been living in one of the residence halls on campus. His family history is unremarkable.

Physical Examination: Findings are as follows: temperature of 103°F, blood pressure of 138/89 mm Hg, heart rate of 90 beats/min, and respirations of 19 breaths/min. Body mass index (BMI) is 24 kg/m^2. His constitutional symptoms include fever and tiredness. He appears anxious. The ear/nose/throat (ENT) and mouth exam is within normal limits, with the exception of mild rhinorrhea. Several cervical lymph nodes are palpable on his anterior neck. His heart rate and rhythm are regular, without murmur or gallop. His lungs are clear, with good air movement throughout.

Laboratory and Diagnostic Findings: A rapid molecular assay result for influenza was negative. Parasite-based diagnostic tools are not readily available at the university health center to rule out *Plasmodium falciparum* infection. His complete blood count (CBC) and complete metabolic panel (CMP) are within normal limits. Results of an HIV fourth-generation test are positive.

CASE STUDY 5.1 QUESTIONS

- *What lab tests should be considered in a first patient visit for possible new HIV infection? If the patient does indeed have a new HIV infection, what are likely to be the lab findings?*
- *Describe the differences between viral infections due to influenza virus and those due to HIV. How would you describe HIV pathophysiology and the appropriate treatment regimen to a new patient?*

CASE STUDY 5.2: A Child With Hand, Foot, and Mouth Disease

Stephanie L. Carper

Patient Complaint: "*My baby was sent home from daycare yesterday because she developed a fever. They told me her temperature was 101, and that she had a rash in her diaper area and behind her knees. She was crying last night, so I gave her some ibuprofen to see if it would bring her fever down.*"

History of Present Illness/Review of Systems: A mother has brought her 18-month-old girl to the clinic today. The child was sent home from daycare yesterday because of illness and was still feverish this morning, with a temperature of 102°F, despite being given ibuprofen the night before. The child has not had any vomiting but woke up crying during the night. Mom is concerned because the child refused water and milk this morning, although she had a wet diaper upon waking. She also notes that the girl seems to be drooling more than usual and had a runny nose this morning.

Past Medical/Social History: The patient was a full-term infant, with a birth weight of 7 lb 10 oz, delivered vaginally, with a normal newborn screen. She has been seen at the clinic for routine well-baby care since birth and has no chronic illnesses and no past surgical history. She lives with her mother, father, and older sister (aged 4 years) in a single-family home and attends daycare full time.

Physical Examination: Findings are as follows: temperature of 99.6°F; heart rate of 118 beats/min; and respiratory rate of 26 breaths/min, with peripheral oxygen saturation of 99%. General: The patient is an alert infant and appears mildly ill but in no apparent distress. Her skin is warm and dry, with coalesced erythematous papules noted bilaterally on the popliteal fossa and across the buttocks, and small, scattered, and annular macular erythematous lesions bilaterally on the palms and soles. Head is normocephalic and atraumatic. Examination of the eyes shows clear sclerae and conjunctivae, with no active discharge; pupils are equal, round, and reactive to light and accommodation (PERRLA); and intact extraocular movements. A moderate amount of clear rhinorrhea is noted, along with moist mucous membranes, pharynx with moderate injection, no tonsillar hypertrophy or exudative tonsils, and a few scattered vesicles on posterior pharynx. There is full range of neck motion, with no cervical lymphadenopathy. Upper extremities have full range of motion, with no gross deformity. Lungs are clear to auscultation bilaterally, with no signs of accessory muscle use or labored breathing. Heart rate and rhythm are regular, with S_1 and S_2 heart sounds present and no murmurs. Abdomen is soft, nontender, and nondistended, with no hepatosplenomegaly. Genitalia are not examined. Lower extremities show full range of motion. Neurological exam reveals an infant who is alert and oriented appropriately for age and development, intact cranial nerves II to XII, normal tone for developmental age, and normal gait for development.

Laboratory and Diagnostic Findings: No tests are warranted for this condition.

CASE STUDY 5.2 QUESTIONS

- *What is the usual course for a mild to moderate acute viral illness, from the prodrome to the resolution?*
- *Hand, foot, and mouth disease can be caused by one of several strains of coxsackievirus. Will a child who has had one episode of this syndrome be protected against future episodes?*

BRIDGE TO CLINICAL PRACTICE

Ben Cocchiaro

PRINCIPLES OF ASSESSMENT

History and Physical Examination

- *Exposure history:* acute illness in family and community contacts, healthcare exposure (especially in older adults), daycare exposures in children, diet, animal contacts (including bites and stings), social history (including travel, substance use, occupational exposure, sexual history, and outdoor activity)
- *Systemic signs and symptoms of infection:* fever, chills, malaise, myalgias, arthralgias, anorexia, vomiting, diarrhea, night sweats, and weight loss
- *Physical examination:* focusing on vital signs (fever, tachycardia, increased respiratory rate) and routes of exposure (eyes, ears, nose, throat, skin, lungs, abdomen, genitalia, lymph nodes)
- *Localized or generalized signs and symptoms of infection:* pain, swelling, redness, heat, rash, rhinorrhea, swollen tonsils (with or without exudate), red pharynx, cough (productive or nonproductive); lung assessment (auscultation for crackles, diminished breath sounds, egophony; palpation for fremitus, percussion for dullness)
- *Vaccination history*

Diagnostic Tools

- Radiography
- CT
- MRI

Laboratory Evaluation

- Complete blood count with differential
- C-reactive protein
- Erythrocyte sedimentation rate
- *Pathogen identification*
  - Microscopy (smears, biopsies)
  - Culture and sensitivity
  - Immune detection (EIA, ELISA, rapid antigen detection, toxin identification)
  - Molecular detection (NAAT)

MAJOR DRUG CLASSES

- *Antibacterials*
  - Cell wall active: penicillins, cephalosporins, carbapenems, monobactams, vancomycin
  - Protein synthesis inhibition: macrolides, clindamycin, linezolid, aminoglycosides, tetracyclines
  - Nucleic acid synthesis and function inhibition: quinolones, trimethoprim/sulfamethoxazole, metronidazole, nitrofurantoin
- *Antivirals:* amantadine, rimantadine, acyclovir, ganciclovir, vidarabine
- *Antiretrovirals:* zidovudine, didanosine, lamivudine, ritonavir, indinavir
- *Antifungals:* azoles, echinocandins, polyenes, flucytosine
- *Antimalarials:* chloroquine, amodiaquine, piperaquine, primaquine, quinine, mefloquine, artemether, artesunate, dihydroartemisinin, pyrimethamine/sulfadoxine, doxycycline, clindamycin

EIA, enzyme immunoassay; ELISA, enzyme-linked immunosorbent assay; NAAT, nucleic acid amplification testing.