

ATYPICAL MANIFESTATIONS OF MEDICAL CONDITIONS IN THE ELDERLY



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Abstract

Background: Because of age-related physiological changes in the body's organ systems, disease presentation has atypical features in the older patient. Moreover, because of the aging population worldwide and the association of chronic disease with advanced age, elderly patients often have multiple co-morbidities, thus complicating the clinical presentation of common disease states.

Purpose: The article aims to educate and update young physicians, both in family medicine and internal medicine, about the atypical manifestations of medical conditions in the elderly population. Through timely recognition of the atypical features of disease states in the elderly, it is hoped that unnecessary investigations and delays in diagnosis will be avoided.

Methods: The authors identified English-language studies on Medline from 1990 to 2012, using terms such as *older*, *elderly*, or *aged*. They combined these terms with the terms *infection*, *pulmonary embolism*, *coronary artery disease*, *congestive heart disease*, *epilepsy*, *Parkinson's disease*, *fluid and electrolyte balance*, *gastrointestinal disease*, *thyroid disease*, *parathyroid disease*, *autoimmune diseases*, *gout*, or *depression*. They also scanned the bibliographies of the review articles and selected relevant articles.

Results: The authors' findings for most of these terms are discussed.

Conclusion: Non-specific clinical manifestations of disease states are common in the elderly. Knowledge of the variability of disease presentation in older adults is essential for accurate diagnosis and management of illness in the elderly.

Résumé

Introduction: Étant donné les changements physiologiques reliés au vieillissement, les maladies se présentent avec des caractéristiques atypiques chez les personnes âgées. De plus, de par l'association entre l'âge avancé et les maladies chroniques, les personnes âgées ont souvent de multiples comorbidités, ce qui complexifie davantage la présentation des maladies communes.

But : Cet article vise plus particulièrement les jeunes médecins, autant ceux pratiquant en médecine familiale qu'en médecine interne, et a pour but d'enseigner et de mettre à jour les connaissances sur les manifestations atypiques des conditions médicales chez les sujets âgés. En effet, via la reconnaissance rapide des manifestations atypiques de la maladie, on souhaite éviter les investigations inutiles et les délais diagnostiques chez les patients âgés.

Méthodologie : Les auteurs ont identifié des études publiées en anglais et parues entre 1990 et 2012, répertoriées sur Medline, en utilisant des termes comme *plus âgé (older)*, *personne âgée (elderly)* ou *âgé (aged)*. Ils ont combiné ces mots avec les termes *infection*, *embolie pulmonaire*, *maladie coronarienne*, *insuffisance cardiaque congestive*, *maladie de Parkinson*, *équilibre liquidien et électrolytique*, *maladie gastro-intestinale*, *maladie thyroïdienne*, *maladie parathyroïdienne*, *maladies auto-immunes*, *goutte* ou *dépression*. Ils ont également lus les bibliographies des articles de revue et ont sélectionné les articles pertinents.

Résultats : Les trouvailles des auteurs concernant la majorité de ces termes sont élaborées dans l'article.

Conclusion: Les manifestations cliniques non spécifiques de la maladie sont fréquentes chez les personnes âgées. La connaissance de la variabilité de la présentation clinique chez les sujets plus âgés est nécessaire au diagnostic et à la prise en charge adéquate de la maladie chez la personne âgée.

The world population is aging. In the United Kingdom over the period 1985–2010, the number of people aged 65 and over increased by 20% to 10.3 million, and in individuals aged 85 and over it doubled over the same period to 1.4 million. Population aging will continue for the next few decades. By 2035, the number of people aged 85 and over is projected to be almost 2.5 times greater than in 2010, reaching 3.5 million and accounting for 5% of the total population. The population over the age of 65 will account for 23% of the total population in 2035.¹

Statistics also indicate that Canada's population will age rapidly until 2031. By 2036, the number of seniors is projected to reach between 9.9 million and 10.9 million, more than double the level of 4.7 million in 2009. Seniors would account for between 23 and 25% of the total population by 2036, nearly double the 13.9% in 2009.²

Physiological changes due to aging result in different pathophysiological responses to foreign stimuli. Reserve capacity reduces in many systems and the regulatory processes become less efficient than in younger people resulting in atypical disease patterns in the elderly. In one study, less than half of elderly patients presented with symptoms consistent with classic medical presentations.³

Moreover, multiple medical problems coexist in the elderly contributing to the atypical presentation. For example, one study showed that those aged 65–74 years suffered from an average of 4.6 chronic conditions, and this increased to 5.8 for those over 75.⁴

In older patients, often the first sign of an acute illness is functional or cognitive decline. Knowledge of specific disease presentations in the elderly is paramount for correct diagnosis and treatment and to avoid complications.

Because of age-related physiological changes in the body's organ systems, disease presentation has atypical features in the older patient. Moreover, because of the aging population worldwide and the association of chronic disease with advanced age, elderly patients often have multiple co-morbidities, thus complicating the clinical presentation of common disease states.

The article aims to educate and update young physicians, both in family medicine and internal medicine, about the atypical manifestations of medical conditions in the elderly population. By timely recognition of the atypical features of disease states in the elderly, it is hoped that unnecessary investigations and delays in diagnosis will be avoided.

Methods

We identified English-language studies on Medline from 1990 to 2012, using terms such as *older*, *elderly*, and *aged*. We combined these terms with the terms *infection*, *pulmonary embolism*, *coronary artery disease* and *congestive heart disease*, *epilepsy*, *Parkinson's disease*, *fluid and electrolyte balance*, *gastrointestinal disease*, *thyroid disease*, *parathyroid disease*, *autoimmune diseases*, *gout*, or *depression*. We also scanned the bibliography of the review articles and selected relevant articles. Inclusion and exclusion criteria would be helpful.

Infection

Cell-mediated immunity declines with aging, resulting in an impaired response to antigens.⁵ Fatigue, anorexia, urinary or fecal incontinence,

recent alteration of mental status, unexplained recurrent falls, loss of physical functional capacity, and non-specific malaise without fever are common symptoms of infection and bacteremia in the elderly. Urinary incontinence was identified as an independent risk factor for nosocomial blood stream infections in older adults.⁶ Infection was the leading cause of acute confusion among older adults in long-term care facilities in one study.⁷ Bacteremic elderly patients have fewer symptoms and signs (mean 6.7 per patient) than the bacteremic young (mean 9.4 per patient).⁸ Forty-eight percent of elderly patients with serious or life-threatening bacterial infections may fail to elicit a febrile response.⁹

According to a retrospective analysis of 332 necropsies, pneumonia was the most frequently missed diagnosis in the elderly.¹⁰ Vital capacity, maximum voluntary ventilation and total lung capacity decrease with age, whereas functional residual capacity increases, resulting in collapse of small airways and air trapping (Figure 1).¹¹ Age-related decrements in chest wall expansion and alveolar elasticity contribute to a diminished cough reflex. Not surprisingly, older patients with community-acquired pneumonia report a significantly lower number of respiratory (cough, dyspnea) and non-respiratory (chills, sweats, chest pain, headache, myalgia) symptoms.¹² In older patients, tachypnea with or without shortness of breath is the most reliable sign of an acute pulmonary condition.¹³ Altered mental status, confusion, and a sudden decline in functional status may be the only symptoms of pneumonia in the elderly. In one study, the classic triad of symptoms of pneumonia – cough, dyspnea, and fever – was observed in only 30.7% of elderly patients.¹⁴ Total white cell count may be normal or marginally elevated despite the presence of left shift. The proportion of patients with pneumonia without a known causative organism also increases with age and no pathogen is identified in 60% of older adults.¹⁵ *Streptococcus pneumoniae* is the most common causative agent of community-acquired pneumonia in the elderly, while *Mycoplasma pneumoniae* is virtually non-existent.¹⁶ Gram-negative bacilli are the predominant organisms in aspiration pneumonia, followed by anaerobic bacteria and *Staphylococcus aureus*.¹⁷

Symptoms of influenza in elderly may not include fever and the symptoms may appear gradually, unlike that in younger patients.¹⁸ Patients with tuberculosis may present with non-respiratory symptoms. Productive cough, night sweats, fever, and hemoptysis were much less common in older patients.¹⁹ Among the elderly, confusion, middle or lower lobe infiltrates in contrast to the classic upper lobe infiltrate, bilateral involvement, and military tuberculosis is more common.^{20,21} The positive purified protein derivative (PPD) test responses are less common in the elderly.

Asymptomatic bacteriuria is common in the elderly and does not require any treatment and has been found in 37% of women and 20% of men.²² Common pathogens causing urinary tract infections (UTIs) in young adults are *Escherichia coli* and *Staphylococcus saprophyticus*. Among the elderly, *E. coli*, *Proteus* species, *Klebsiella* species, and *Enterobacter* species are common. *S. saprophyticus* is distinctly unusual as a cause of UTIs in the elderly.²³ Like any other infection, UTIs may present with atypical symptoms, such as worsening or new-onset incontinence, lethargy, or confusion. Increased urinary frequency or

Physiologic Changes Due to Aging

Pneumonia

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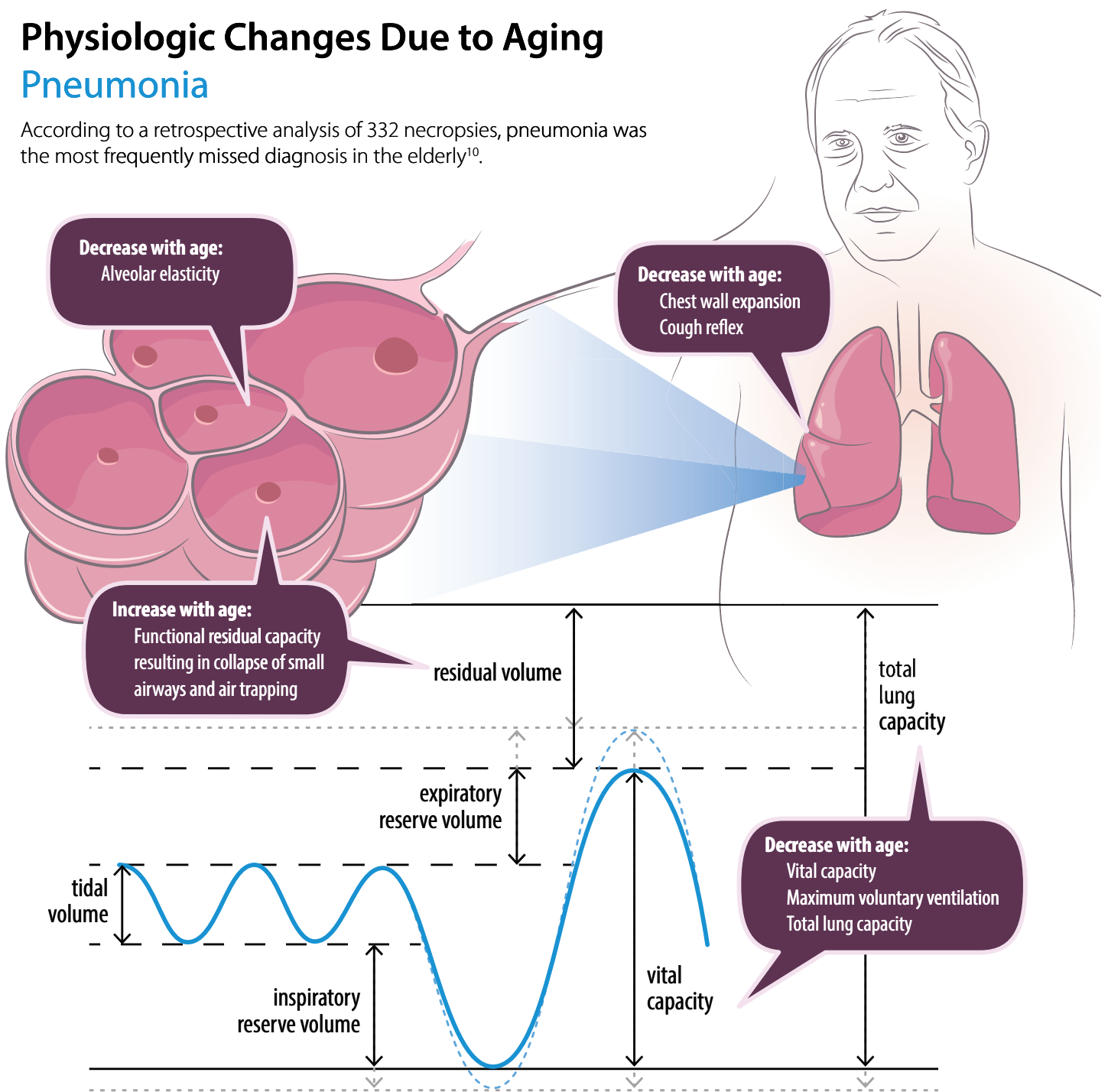


Figure 1. Physiologic changes due to aging: pneumonia.

urgency may not be present in the elderly and urinalysis may not show a large number of white cells. However, a combined negative predictive value of negative urinary leukocyte esterase and nitrites approaches 100% and helps to differentiate UTIs from asymptomatic bacteriuria and other infections.²⁴

The incidence of meningitis falls as we grow old.²⁵ Neck stiffness may be a false positive sign of meningitis in the elderly, as it is common in patients with dementia, cerebrovascular disease and Parkinson's disease.²⁶ *S. pneumoniae* is the most common pathogen causing bacterial meningitis in the young and elderly, with meningococcal and *Haemophilus influenzae* meningitis virtually non-existent in the elderly.²⁷ *Listeria monocytogenes* may be a cause in the elderly, thus the importance of adding ampicillin or penicillin G to a third generation cephalosporin in suspected bacterial meningitis.

Older patients with infective endocarditis are less likely to have classic findings, such as splenomegaly, Osler's nodes, Janeway lesions, and conjunctival hemorrhages.²⁸ Transthoracic echocardiogram (TTE) is less likely to detect vegetations in the elderly and transesophageal echocardiogram (TEE) is more frequently required for diagnoses in these patients.²⁹ The sensitivity of TTE is 75% in younger patients but only 45% in elderly.³⁰

Unlike the young, pyrexia of unknown origin (PUO) can be diagnosed in higher proportion of elderly patients.³¹ In many cases, PUO in the elderly is the result of atypical presentations of common diseases. Temporal arteritis and polymyalgia rheumatica are the most frequent causes of PUO. Among infections, tuberculosis is a more common cause of PUO in the elderly.³² PUO in the elderly has a higher diagnostic yield than in the younger population, infection (particularly tuberculosis) being the most common cause, followed by inflammatory multisystem disease (temporal arteritis) and neoplastic disease.³³

Sensitivity and specificity of blood cultures is not influenced by age.³⁴ The relationship between age and antimicrobial resistance in blood stream infections varies by organism. Blood stream infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) are more prevalent in the elderly.³⁵ However, vancomycin resistant enterococcal infections are not.³⁶

Pulmonary Embolism

The incidence of venous thromboembolism increases with age. The annual incidence of venous thromboembolism is 3.5 per 1,000 in individuals aged 60 to 74 but triples to 9 per 1,000 in individuals 75 and over.³⁷ Older patients may present atypically with acute pulmonary embolism (PE). Moreover, increasing prevalence of alternative cardiopulmonary conditions may mimic PE in the elderly, potentially leading to delays in diagnosis and treatment. Syncope is a particularly important symptom of acute PE in older persons. In one study 24% of older persons but just 3% of younger persons presented with collapse. Older persons less often complained of pleuritic chest pain and hemoptysis and were more often cyanosed and hypoxic.³⁸

Coronary Artery Disease and Congestive Heart Disease

The prevalence of coronary artery disease and congestive heart failure

increases with age. The spectrum of presentation of acute myocardial infarction (AMI) also changes. Chest pain or discomfort is less frequent, while syncope, shortness of breath and acute confusion are more common and sometimes the sole presentation.³⁹ In another study, the proportion of AMI without noticeable chest pain rose statistically significantly from 6% in patients <75 years to 21% in patients ≥ 75 years.⁴⁰ Among elderly with unstable angina, arm pain and sweating were reported significantly less often ($p < .05$).⁴¹ Left ventricular remodelling post-STEMI is more severe in the elderly.⁴² The prevalence of diastolic heart failure increases with age.⁴³ The most common cause of heart failure in the elderly is hypertension, whereas coronary artery disease is the major cause in middle-aged patients. Older patients with cardiac failure may not complain of dyspnea until heart failure is quite advanced. Fatigue may be the only prominent feature. This may be due to an age-related decrease in myocardial compliance resulting in lower cardiac output for any given left ventricular end-diastolic pressure.

Epilepsy

Complex partial seizures are the most common seizure types after the age of 60, accounting for 70% of cases.⁴⁴ The dendritic processes of neurons of cortical layer V are involved in the intracortical communication between adjacent areas of the brain.⁴⁵ Advanced age is associated with a disproportionate loss of dendritic processes of neurons of cortical layers III and V. This may explain why partial seizures in the elderly have fewer propensities to spread to adjacent areas and generalize.^{45,46} Seizures may arise from areas typically not involved in the genesis of seizures in younger patients (mesial temporal and orbito-frontal). Therefore, psychic symptoms and automatism are also less likely.^{43,44} Conversely, sensory and motor symptoms are more common manifestations of seizures due to the involvement of motor and sensory cortices secondary to cerebrovascular disease. Postictal deficits may also be unusually long, lasting for several hours or days.⁴⁶

Parkinson's Disease

The prevalence of Parkinson's disease (PD) increases with age, given that age is the single most important risk factor.⁴⁷ Bradykinesia, rigidity, tremor, and problems of gait and balance are commonly found in elderly people without any neurological illness. These may be difficult to differentiate from early PD.⁴⁸ Non-motor symptoms of PD like constipation, incontinence, falls, orthostatic hypotension, sweating abnormalities, dysphagia, dribbling, and psychiatric disorders may be more common at presentation.

Gastrointestinal Disease

The incidence of gastroesophageal reflux disease (GERD) and its complications increase substantially with age. Compared with younger individuals, older patients with GERD have more severe mucosal disease but present with only mild or no symptoms at all due to poor pain perception.⁴⁹ Older individuals with GERD may have greater respiratory involvement.⁵⁰ There is a higher prevalence of *Helicobacter pylori* in the elderly and as the prescribing of NSAIDs increases. It is not therefore surprising that gastric ulcers are common in the elderly. The prevalence of gastric ulcer in male and female patients aged ≥60

Physiologic Changes Due to Aging Thyroid Disease

Classic signs of hyperthyroidism, such as tremor, irritability, and nervousness, are often absent in older patients. Apathetic features, such as fatigue, weight loss, lethargy, palpitations, congestive cardiac failure, or atrial fibrillation, may be present but go unrecognized because they are inadvertently attributed to other age-prevalent problems.

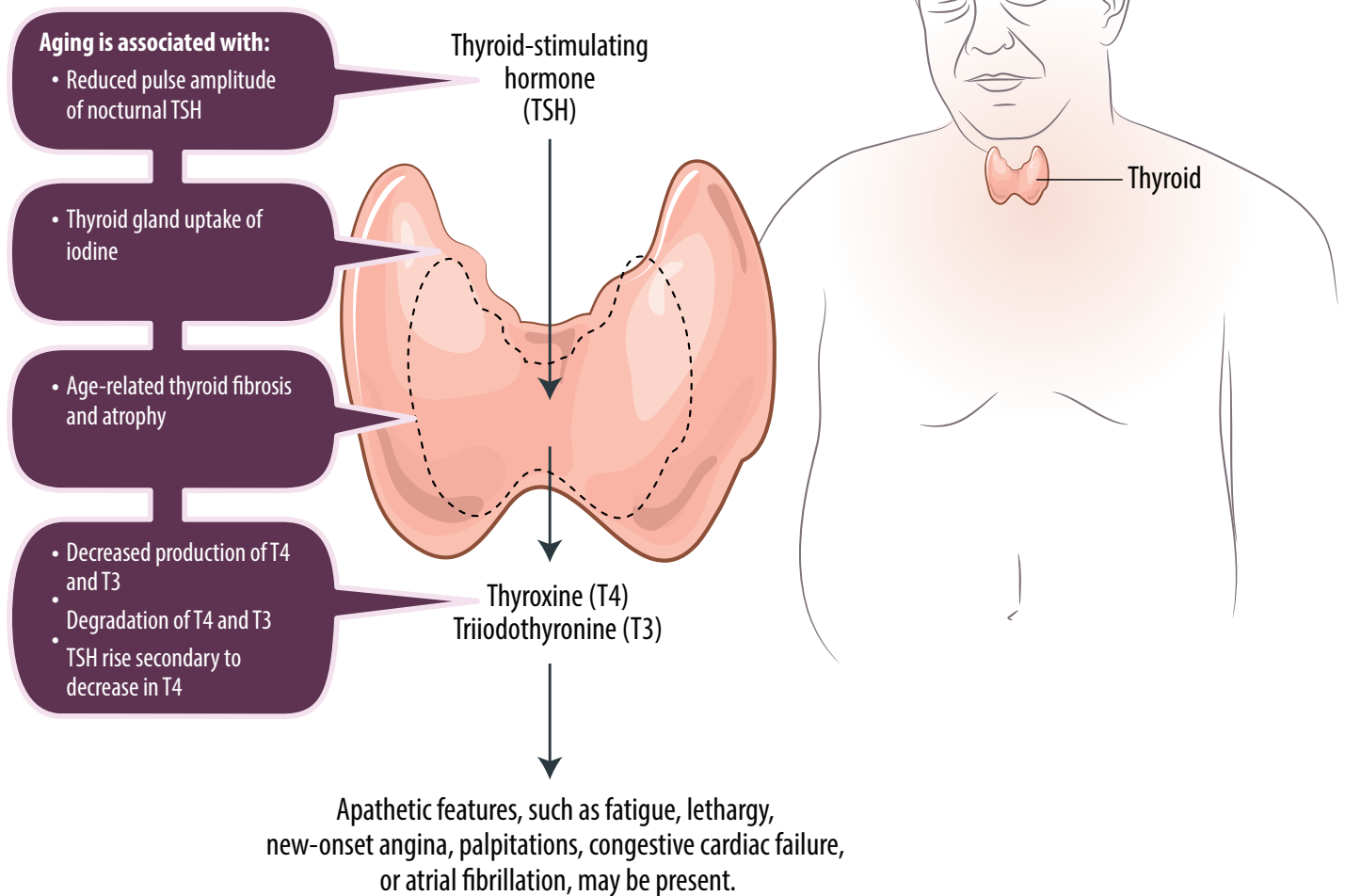


Figure 2. Physiologic changes due to aging: thyroid disease.

years (17.24% and 14.80%, respectively) is markedly higher than that in male and female patients aged <60 years (7.57% and 4.17%, respectively) ($p < 0.001$).⁵¹ However, the association with *H. pylori* is less strong, with 35% of non-NSAID ulcers being *H. pylori* negative in one study.⁵² Gastric and duodenal ulcers also tend to be larger.⁵³ The risk of developing ulcers and their complications also rises irrespective of NSAID use.⁵⁴

Many studies have also suggested that ulcer pain is less common than in younger patients.⁵⁵⁻⁵⁷ In one study, typical abdominal pain was often missing and the ulcer often presented with gastrointestinal bleeding.⁵⁸ In another, 34 consecutive patients with unrecognized intra-abdominal perforation were identified from post-mortem records. Elderly obese women are at particular risk. This diagnosis should be considered especially in the presence of unexplained tachycardia, hypotension, or pyrexia.⁵⁹

Thyroid Disease

Aging is associated with decreased production of T4 and T3, degradation of T4 and T3, reduced pulse amplitude of nocturnal TSH, thyroid gland uptake of iodine and TSH rise secondary to a decrease in T4 (Figure 2).⁶⁰ Classic signs of hyperthyroidism, such as tremor, irritability, and nervousness, are often absent in older patients. Apathetic features, such as fatigue, anorexia, weight loss, lethargy, new-onset angina, palpitations, congestive cardiac failure, or atrial fibrillation, may be present. In one study, the most frequent signs found in the elderly were tachycardia, fatigue, and weight loss. Hyperactive reflexes, increased sweating, heat intolerance, tremor, nervousness, and increased appetite were rare.⁶¹ Age-related relative resistance to thyroid hormone action may underlie the paucity of symptoms in hyperthyroidism.⁶² Because of age-related thyroid fibrosis and atrophy, as many as 20% of hyperthyroid elderly patients fail to have either an enlarged or palpable thyroid gland. Moreover, ophthalmologic findings are frequently absent.⁶³

Hypothyroidism in the elderly often escapes recognition because many clinical signs and symptoms associated with hypothyroidism such as lethargy, changes in cognition, and constipation are inadvertently attributed to other age-prevalent problems.⁶⁴

Parathyroid Disease

Classic presentations of hypercalcemia, such as renal colic,

gastrointestinal pathology, and skeletal disease, are less common in the elderly. An acute confusional state with or without volume depletion is a more frequent presentation.⁶⁵ Parathyroid hormone levels have also been found to be higher. This may be due to a decline in parathyroid hormone stimulation of 1,25-dihydroxyvitamin D, which leads to decreased calcium absorption and mild secondary hyperparathyroidism.⁶⁶

Serum albumin falls with age; however, significant hypoalbuminemia is more commonly due to disease than aging. Therefore, in elderly patients, hypoalbuminemia is the most common cause of hypocalcemia.

Autoimmune Diseases

The diagnosis of autoimmune diseases in the elderly may be difficult because of their insidious presentation, atypical features, and a high prevalence of autoantibodies. Antiphospholipid antibodies are found in 63.6%, rheumatoid factor in 47.7%, and anti-double-stranded DNA antibodies in 29.5% of the healthy elderly population.⁶⁷ There is a tendency for decreased rheumatoid factor seropositivity in rheumatoid arthritis.⁶⁸ Involvement of proximal joints may mimic polymyalgia rheumatica while a high frequency of normal creatine kinase levels in polymyositis and dermatomyositis may delay diagnosis.^{69,70}

Gout

In classic gout, the initial attack is acute monoarthritis, with predominant involvement of lower extremity joints, especially the first metatarsophalangeal joint. Tophaceous deposits typically occur over the elbows, fingers, or ears, and chronic polyarticular arthritis may develop. In the elderly, polyarticular attacks are more frequent, with involvement of upper extremities, and have a sub-acute to chronic, more indolent course. There is an increased incidence of tophi, which appear earlier in the disease and often in atypical locations.⁷¹ There is a male preponderance in younger patients but women constitute half of patients with disease onset after age 60 and almost all after age 80.⁷² A slight age-related increase in serum uric acid has been reported.⁷³ Polyarticular gouty arthritis in the elderly may be mistaken for nodular rheumatoid arthritis.⁷⁴ The distinguishing features include asymmetric presentation, inflammation in different phases in different joints, and radiological findings of asymmetric soft tissue tophaceous swellings, and marginal and periarticular punched out erosions with overhanging edges. Gouty arthritis and tophi may also be superimposed on osteoarthritic Heberden's and Bouchard's nodes. Examination of the radiographs and analysis of aspirate for crystals will lead to a correct diagnosis.

Conclusion

Older adults are the largest user of health care resources. Nonspecific clinical expressions of disease are common in the elderly, and a heightened awareness of these manifestations will assist in avoiding the pitfalls of a misdiagnosis and will likely lead to better outcomes.

This article was peer reviewed.

Conflict of interest: None declared.

Key Points

- *Because of age-related physiological changes in the body's organ systems, disease presentation has atypical features in the older patient.*
- *Due to the aging population worldwide and the association of chronic disease with advanced age, elderly patients often have multiple co-morbidities, thus complicating the clinical presentation of common disease states.*
- *With timely recognition of the atypical features of disease states in the elderly, it is hoped that unnecessary investigations and delay in diagnosis will be avoided.*

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