FEVER IN THE OLDER ADULT (OR NOT)

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CPD Geriatrics Day

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- AGS teaching slides – Infectious Diseases
- Pat Montgomery
- CGS Covid website

Faculty/Presenter Disclosure

- **Faculty: Phil St John**

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  - **Board: Age and Opportunity (non remunerated)**

  - **I am a geriatrician**

Disclosure of Commercial Support

- **I am unaware if this program has received financial or in-kind support from any outside organization.**

- **Potential for conflict(s) of interest:**
  - Phil St John has not received payment/funding, etc. from an organization supporting this program AND/OR organization whose product(s) are being discussed in this program.

Mitigating Potential Bias

Not applicable.

ACKNOWLEDGEMENTS

- AGS Teaching slides
- Pat Montgomery

Mr F

- 87 year old gentleman, living in rooming house on Furby
- Past Hx: Hypertension, COPD, smoking, generous alcohol use, past hepatitis
- In to ER with “dyscopia” – sent home
- Returned 6 hours later with falls and “dyscopia”
- “Failed OT and PT” – admitted non teaching
- Afebrile, exam “normal”

COURSE IN HOSPITAL

- 12 hours later – spiked temp to 38.7
- Looked unwell, O2 sats 90% on RA, RR 32, JVP not seen. RLL crackles
- WBC 14.2 no left shift
- CXR RLL infiltrate

- This was Internal Medicine Grand Rounds Case from Dec 5, 2001

KEY POINTS

- Older adults are heterogeneous
- On average, febrile response is blunted
- On average, there are more atypical presentations of sepsis
- Fever needs to be acted upon
- No fever is not reassuring
- Changes from baseline are critical

COVID – not the focus of this talk

- ***COVID is the most important pandemic in our lives***
- Already had CPD on this
- DO NOT FORGET COVID
- COVID has atypical presentations
  - Falls
  - Functional decline
  - Delirium
  - Decreased appetite
- May not present with fever

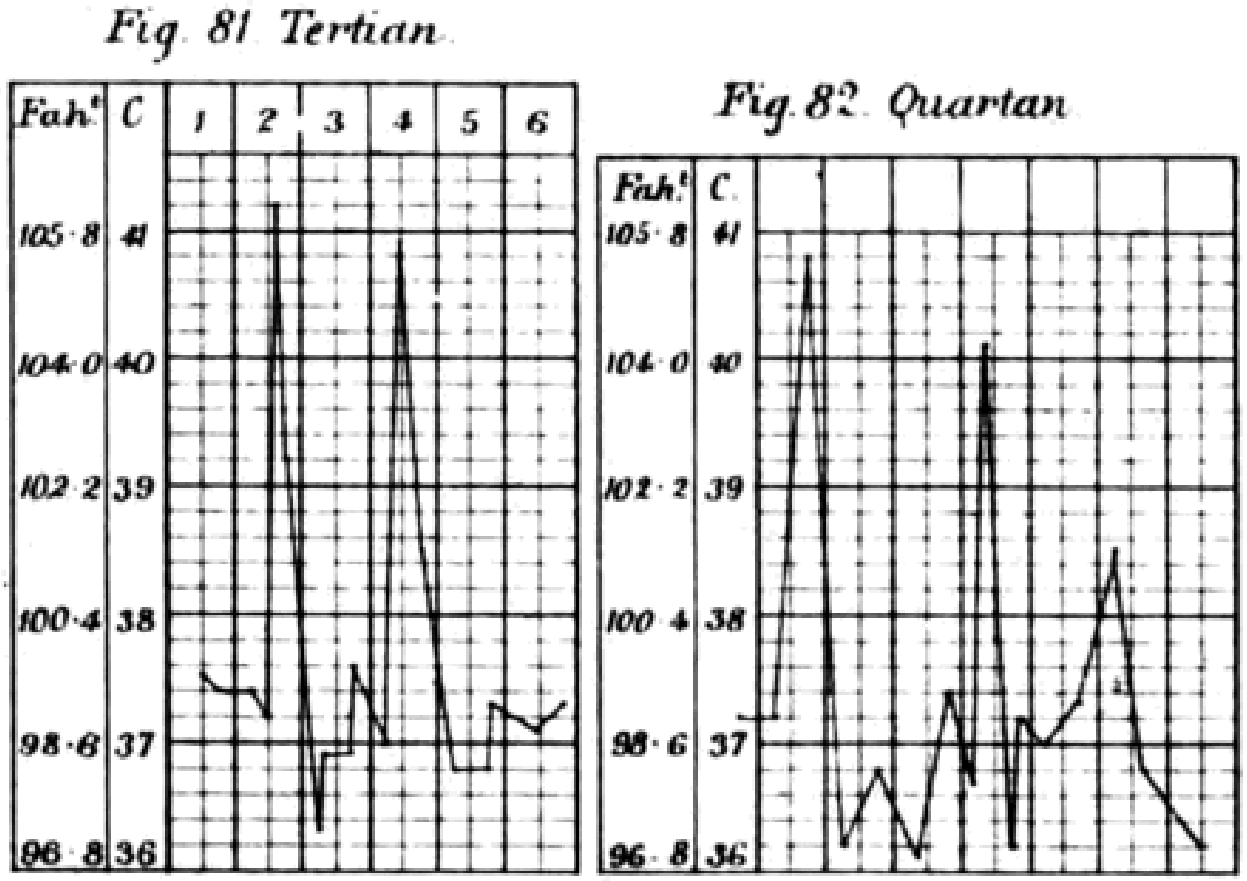
HISTORICAL CONTEXT

- Fever well established in Hippocratic writings
  - “Fever comes about from the following: whenever bile or phlegm is heated, all the rest of the body is heated along with them, and this is called fever”
  - Fever due to disease, not a problem unto itself
  - Different diseases had different patterns of fever
  - No distinguishing between symptom and sign

- Avicenna:
  - “Fever is a foreign heat that starts in the heart and, with the flow of blood, spreads through the arteries and veins, and in the end the entire body becomes so hot that it can not perform its normal functions.”
  - Four stages
  - Linking to rapid and strong pulse (Second phase)

- Wunderlich (1868)
  - Accurate thermometers
  - Approximately 1 million temperature measurements obtained in 25 000 patients during a 16-year period

Figure 1. Fever curves for tertian and quartan fevers; x-axis represents time, and y-axis, temperature (from ...



Clin Infect Dis, Volume 55, Issue 7, 1 October 2012, Pages 976–980, https://doi.org/10.1093/cid/cis596

DEFINITIONS - inconsistent

- **Fever**
  - Is an elevation in core body temperature above the daily range for an individual – due to a change in thermoregulation
  - An elevation of body temperature (>37.2°C/98.9°F in the morning and >37.7°C/99.9°F in the evening) in conjunction with an increase in the hypothalamic set point (Harrison's, 2020)

- **Hyperthermia** -An uncontrolled increase in body temperature that exceeds the body's ability to lose heat *without* a change in the hypothalamic set point. Hyperthermia does not involve pyrogenic molecules.

- **Hyperpyrexia** — Hyperpyrexia is the term for an extraordinarily high fever (>41.5°C)

- *Fever of unknown origin (FUO):* Temperatures >38.3°C (>101°F) on two or more occasions and an illness duration of ≥3 weeks, with no known immunocompromised state and unrevealing laboratory and radiologic investigations into the cause

- In most adults, an oral or axillary temperature above 37.6°C (99.7°F) or a rectal or ear temperature above 38.1°C (100.6°F) is considered a fever.

Peripheral Temperature

- For detection of fever (bivariate random-effects meta-analysis), sensitivity was low (64% [95% CI, 55% to 72%]; I2 = 95.7%; P <0.001) but specificity was high (96% [CI, 93% to 97%]; I2 = 96.3%; P <0.001).

- Only 1 study reported sensitivity and specificity for the detection of hypothermia.

- Different methods and sites give different readings – STICK WITH ONE METHOD

Ann Intern Med. 2015;163(10):768.

WHAT IS DIFFERENT ABOUT OLDER ADULTS?

- Increased heterogeneity
- Aging – related changes
- Previous exposures
  - Latent infections – eg TB
  - Previous immunity
- Higher comorbidity burden
- More likely to live in a congregate setting
- Often different activities related to exposure

AGE-RELATED ALTERATIONS IN IMMUNE FUNCTION

- Immune response declines with age, a phenomenon known as ***immunosenescence***
- The main features are depressed T-cell responses and depressed T-cell/macrophage interactions
- B cells produce antibodies with lower affinity → weakened immunogenicity of vaccines

IMPACT OF COMORBIDITY ON IMMUNE FUNCTION

- The impact of comorbidities on innate immune function and host resistance is greater than the impact of age itself

- Comorbid diseases also indirectly complicate infections (eg, community-acquired pneumonia in an older adult with multiple comorbidities often requires hospitalization)

IMPACT OF NUTRITIONAL STATUS ON IMMUNE FUNCTION

- On hospital admission, global undernutrition is present in 30%–60% of patients ≥65 years
- 11% of older outpatients are protein calorie malnourished, mostly due to reversible conditions such as depression, poorly controlled diabetes mellitus, environmental factors (eg, access to food) and medication side effects
- Some nutritional interventions may boost immune function in older adults, but results vary with the population studied and the supplements used

LONG-TERM CARE CONSIDERATIONS

- Residence in a LTCF puts older adults at risk of epidemic diseases
- Widespread antibiotic use increases likelihood of infection by antibiotic-resistant organisms
- Resistance issues are worsened by:
  - Frail host
  - Close proximity of residents
  - Poor staff adherence with prevention strategies (eg, influenza immunization)
  - Overutilization of antibiotics
  - Difficulties with infection control implementation
- Maintaining up-to-date immunizations is critical

ATYPICAL PRESENTATION

- Older adults may present without typical signs and symptoms, even if the infection is severe
- Fever may be absent in 30%–50% of older adults with serious infections
- Fever in older nursing-home residents can be redefined as:
  - Single oral temperature >100°F (37.8°C), or
  - Temperature >2°F (1.1°C) over baseline, or
  - Oral temperature >99°F (37.2°C) on repeated measures, or
  - Rectal temperature >99.5°F (37.5°C) on repeated measures

ANTIMICROBIAL MANAGEMENT

- Drug distribution, metabolism, excretion, and interactions can be altered with age
- Even in the absence of disease, aging is associated with a reduction in renal function
- Antibiotic interactions occur with many medications commonly prescribed for older adults
- Risk factors for poor medication adherence include poor cognitive function, impaired hearing or vision, co-prescription of multiple medications, and financial constraints

HISTORY

- Complete
- Collateral with as many sources as possible
- Chronology of events
- Symptoms **(including atypical)**
- **Sick contacts**
- **Travel**
- Medications (complete)
- Pets
- Prostheses

Physical examination

- Consistent measurement and site for temperature
- ***REALLY*** do respiratory rate and pulse
- Don’t forget pressure sores, joints (all), myalgiae, temporal artery tenderness, cardiac examination, skin, and mental state examination

LAB

- Depends upon situation, history and physical, values of patient/family
- General minimum – CBC, ESR or CRP

TREATMENT

- Find and treat the cause
- Antipyretics
  - Usually, unless there is a need to establish effectiveness of treatment
  - Relieves symptoms

BACTEREMIA AND SEPSIS

- Older patients with bacteremia are less likely than younger adults to have chills or sweating, and fever is may be absent
- GI and genitourinary sources of bacteremia are more common than in younger adults
- Mortality rate with nosocomial gram-negative bacteremia: 5%–35% in younger adults, 37%–50% in older patients

PNEUMONIA: EPIDEMIOLOGY

- Patients ≥ 65 account for over 50% of cases
- Cumulative 2-year risk for nursing home residents is about 30%
- Mortality in older patients is 3-5X that of younger adults
- Comorbidity is the strongest independent predictor of mortality
- Swallowing problems likely a risk (dementia, parkinsonism, stroke, etc.)

CAUSES OF PNEUMONIA IN OLDER ADULTS

- *Streptococcus pneumoniae* predominates
- Gram-negative bacilli (eg, *Haemophilus influenzae, Moraxella catarrhalis, Klebsiella* spp.) are more common than in younger adults, particularly in those with COPD and those residing in LTCF
- *Staphylococcus aureus* and respiratory viruses are also causes of pneumonia in long-term care residents

COMMUNITY-ACQUIRED PNEUMONIA

Infectious Diseases Society of America guidelines suggest the following as first-line therapy for adults over 60, with or without comorbidity:

- β-lactam/β-lactamase combination or advanced-generation cephalosporin, with or without a macrolide
- Alternatively, one of the newer fluoroquinolones with enhanced activity against *S. pneumoniae*

NURSING HOME AND HOSPITAL-ACQUIRED PNEUMONIA

- Initial regimens should be broadly inclusive, followed by step-down therapy to narrower coverage if the causative agent is identified
- For MRSA-colonized patients or patients in units with high rates of MRSA, initial regimens should include vancomycin or linezolid until MRSA is excluded (NOT YET MANITOBA)
- Patients with improving hospital-acquired pneumonia not caused by nonfermenting gram-negative bacilli (eg, *Pseudomonas, Stenotrophomonas*) can receive short courses of antibiotics (8 days)

REDUCING THE RISK OF PNEUMONIA

- Immunization
- Smoking cessation
- Manage comorbidities (eg, minimizing aspiration risk in post-stroke patients, limited use of sedative hypnotics)
- System changes with attention to infection control may be particularly effective in LTCF

INFLUENZA

- Annual flu vaccination is recommended for all adults
  - FDA approved high-dose vaccine for adults ≥ 65 yr, which produces higher antibody responses and appears to be more effective compared to standard dose for preventing influenza in this age group
  - Treatment with neuraminidase inhibitors is most effective if initiated within 48 hours of symptom onset
- Oseltamivir (oral) is easier to use than zanamivir (inhaled)

URINARY TRACT INFECTION (UTI)

- One of the most common ID related diseases
- Gram-negative bacilli are most common uropathogens identified in urine cultures of older adults
- Older adults are more likely to have non- *Escherichia coli* gram-negative rod isolates (eg, *Pseudomonas* spp.*)* and to have resistance against commonly prescribed oral antibiotics compared to younger adults
- Additional organisms in patients with indwelling catheters include enterococci, *S. aureus,* and fungi, particularly *Candida* spp.

ASYMPTOMATIC BACTERURIA

- Affects up to 20% of women in the community and 25-50% of women in LTCF
- Incidence in men is approximately half that in women
- **Treatment is not recommended**
  - No clinical benefit
  - Associated with adverse effects, expense, *C. difficile* colitis, and potential for selection of resistant organisms

CHOOSING WISELY®

- Don’t use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present.

LOWER-TRACT UTI (CYSTITIS) IN OLDER WOMEN

- Characterized by dysuria, new or worsening frequency, and urgency
- 3–7 days of therapy sufficient for uncomplicated cystitis
- Numerous treatment options depending upon local resistance patterns

UPPER-TRACT UTI (PYELONEPHRITIS) IN OLDER WOMEN

- Characterized by fever, chills, nausea, and flank pain; commonly accompanied by lower-tract symptoms
- Requires 7–21 days of therapy
- Consider IV antibiotics for patients with suspected urosepsis, those with upper tract disease due to relatively resistant bacteria, and those unable to tolerate oral medications
- Culture and sensitivity data should be obtained

UTI IN OLDER MEN

- Causative organisms and treatment choices are similar to those for older women
- Usually due to obstructive prostatic disease or functional disability; ≥7 days of therapy needed
- If prostatitis is suspected, ≥6 weeks of therapy is usually required
- Culture and sensitivity data should guide therapy for virtually all UTIs in older men

UTI IN LONG-TERM CARE RESIDENTS

- In patients who are cognitively impaired, it is important to carefully assess for new or worsening symptoms such as urinary incontinence, physical signs such as suprapubic tenderness, and to consider other diagnoses that may be responsible for non-specific symptoms (eg, medications, dehydration, constipation).

- However, if non-specific symptoms (eg, mental status changes) persist despite other interventions (hydration, treatment of constipation), obtaining urine studies to evaluate for UTI is reasonable.

RECURRENT UTI

- Antibiotics for prevention not recommended in older women unless other strategies ineffective
- Cranberry capsules have not shown to prevent bacteriuria in nursing home residents

INFECTIVE ENDOCARDITIS

- In older adults, associated with degenerative valvular disorders and prosthetic valves
- Treatment is IV antibiotics for 4–6 weeks
- Consider surgery for severe valvular dysfunction, recurrent emboli, marked heart failure, myocardial abscess, fungal endocarditis, or failure of antibiotics to sterilize blood cultures

PROSTHETIC DEVICE INFECTIONS

- Device removal usually required for cure
- Early and prolonged antibiotic intervention (for months), combined with aggressive surgical drainage, may be successful if symptoms have been present only for a brief duration
- When full functionality is the goal, the best course is device removal and administration of antibiotics for 6–8 weeks, followed by reimplantation
- Administration of prophylactic antibiotics other than for heart valves remains controversial

SEPTIC ARTHRITIS

- More likely in joints with underlying pathology
- Early arthrocentesis is indicated in any mono- or oligoarticular syndrome, to exclude infection
- *S. aureus* is the most likely pathogen
- Aggressive antibiotic therapy should be combined with serial arthrocentesis in uncomplicated cases
- Surgical drainage required when conservative strategy fails

OSTEOMYELITIS

- *S. aureus* is the predominant organism
- GI and genitourinary flora are more common than in younger adults, so a specific microbiologic diagnosis is useful
- Infections of pressure ulcers and diabetic foot infections commonly require surgical consultation plus aggressive antimicrobial therapy aimed at mixed aerobic and anaerobic bacteria

BACTERIAL MENINGITIS

- Older adults account for most meningitis-associated fatalities
- Very broad spectrum antibiotics are recommended as empiric therapy until a specific isolate can be tested for antimicrobial susceptibility
- Ampicillin is the drug of choice for Listeria spp.

GASTROINTESTINAL INFECTIONS

- Can present diagnostic challenges in the absence of fever or elevated WBC counts; a high index of suspicion is necessary
- Diagnostic aids:
  - Intra-abdominal infection—CT or labeled WBC study
  - Cholecystitis, appendicitis, abscess—ultrasound
  - Ischemic bowel—often requires angiography or flexible sigmoidoscopy
- Treat *infectious diarrhea* as in younger adults

CLOSTRIDIUM DIFFICILE INFECTION (1 of 2)

- Recent increase in incidence and severity, especially in older adults
- Hypervirulent strain, NAP1/BI/027 implicated in outbreaks
  - Associated with use of clindamycin, third generation cephalosporins, and fluroquinolones
- Diagnosis made with PCR for B toxin gene, or using antigen detection for the *C difficile* antigen followed by A/B toxin assay

CLOSTRIDIUM DIFFICILE INFECTION (2 of 2)

- Antibiotic stewardship reduces C Diff infections (Baur et al, 2017)
- Discontinue offending antibiotics
- First-line treatment:
  - Oral vancomycin (use of metronidazole has been associated with treatment failure) – although effect size is small (Goldenberg et al, 2017).
- Multiple relapses occur in >25% of older adults
- FMT has been used in persons with severe recurrence that is not responsive to antibiotics

FEVER OF UNKNOWN ORIGIN

- Defined as temperature >38.3°C (101°F) for at least 3 weeks, undiagnosed after 1 week of medical evaluation
- About one third of cases are due to treatable infections, especially intra-abdominal abscess, bacterial endocarditis, and tuberculosis
- Collagen vascular diseases are more common causes than in younger patients (about 30% of cases)
- Neoplastic disease accounts for another 20% of cases

FUO

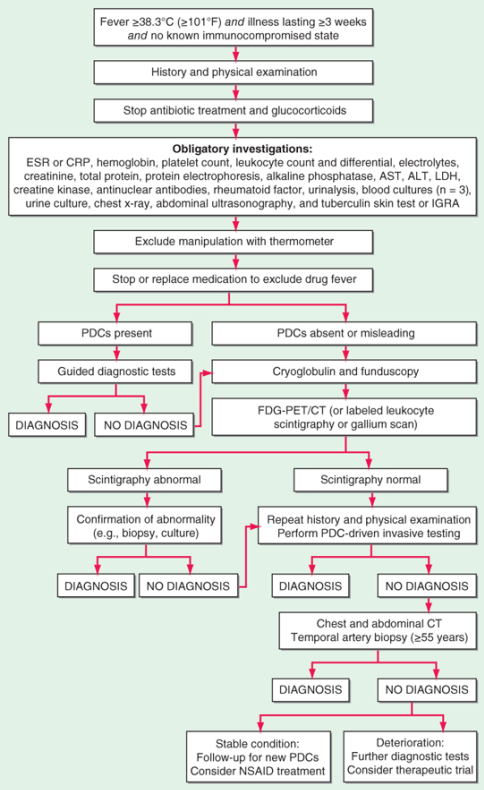
- Atypical presentation
  - Endocarditis,
  - Diverticulitis,
  - Vertebral osteomyelitis,
  - Extrapulmonary tuberculosis
- The most common NIIDs
  - Large-vessel vasculitis,
  - Polymyalgia rheumatica,
  - Sarcoidosis,
  - Collagen Vascular Disease
- Neoplasms,
  - Lymphoma - Fever occasionally precedes lymphadenopathy detectable by physical examination

SUMMARY

- Immune function and host resistance are compromised in older adults as a consequence of both immune senescence and comorbid disease
- A redefinition of fever should be considered in the frail older patient
- There are suggested criteria for initiating antibiotic therapy in residents of long-term-care facilities
- Careful selection of first-line therapy is warranted in older patients with pneumonia

KEY POINTS

- Atypical presentations are common
- Absence of fever does NOT indicate a lack of sepsis or infection
- Other causes of fever should be considered in some settings



Source: J.L Jameson, A.S. Fauci, D.L. Kasper, S.L. Hauser, D.L. Longo, J. Loscalzo: Harrison's Manual of Medicine, Twentieth Edition.

Structured approach to pts with fever of unknown origin (FUO). ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FDG-PET/CT, 18F-fluorodeoxyglucose positron emission tomography combined with low-dose computed tomography; IGRA, interferon γ release assay; LDH, lactate dehydrogenase; NSAID, nonsteroidal anti-inflammatory drug; PDCs, potentially diagnostic clues (all localizing signs, symptoms, and abnormalities potentially pointing toward a diagnosis).

EVALUATING FEVER OF UNKNOWN ORIGIN IN OLDER ADULTS (1 of 2)

1.	Confirm fever; conduct thorough history (include travel, MTB exposure, drugs, constitutional symptoms, symptoms of giant cell arteritis) and physical exam. Discontinue nonessential medications.
2.	Initial laboratory evaluation: CBC with differential, liver enzymes, ESR, blood cultures × 3, PPD skin testing, TSH, antinuclear antibody. Consider antineutrophilic cytoplasmic-antibody or HIV-antibody testing.
3.	a) Chest or abdomen or pelvic CT scan—if no obvious source; or b) Temporal artery biopsy—if symptoms or signs are consistent with giant cell arteritis or polymyalgia rheumatica and increased ESR; or c) Site-directed work-up on basis of symptoms or laboratory abnormalities, or both.

EVALUATING FEVER OF UNKNOWN ORIGIN IN OLDER ADULTS (2 of 2)

4.	If 3a is performed and no source is found, then 3b, and vice versa.
5.	a) BM biopsy—yield best if hemogram abnormal—send for H&E, special stains, cultures, or b) Liver biopsy—very poor yield unless abnormal liver enzymes or hepatomegaly.
6.	Indium-111 labeled white blood cell or gallium-67 scan—nuclear scans can effectively exclude infectious cause of FUO if negative.
7.	Laparoscopy or exploratory laparotomy.
8.	Empiric trial—typically reserved for antituberculosis therapy in rapidly declining host or high suspicion for tuberculosis (ie, prior positive PPD).