Interpreting laboratory results in the elderly

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Family medicine refresher course

November 26 2018

Declaration

- "I (we) declare that I have no conflicts of interest in the authorship of this contribution."

Reference ranges in the elderly

- Notion of reference ranges
- Effect of aging on the body
- Impact of aging on commonly measured analytes

Oldest Living Human Being of All Time Published 18 August 2015

Jeanne Calment (1875–1997) of France, who died at the age of 122 years, 164 days.

Definitions

- “Aging: a process of gradual and spontaneous change, resulting in maturation through childhood, puberty, and young adulthood and then decline through middle and late age.”

Case #1

- 85 year old female recently admitted to a long- term facility with progressive weakness.
- Now complains of vomiting
- On exam MD palpates an abdominal mass
- CT scan⇒ mass, likely benign
- Na: 119 mmol/L

Case #2

- An 81 year old woman presents to the ER with a new onset of chest pain.
- Investigation reveals a Hb of 100 g/L.
- Is she anemic?

Case #3

- 75 year old male undergoes annual physical.
- He has no complaints
- among many other tests Alkaline phosphatase is oredered.
- Results: Alk Phos:145U/L

Case # 4

- A 77 year old male complains of vague abdominal discomfort for the past 2 months.
- You order a C-reactive protein. The result is 15 mg/L.(RR<10mg/L)
- ESR: 40mm/h
- Do you investigate to rule out an underlying malignancy?

Reference ranges

- Interpretation of clinical laboratory data is a comparative decision-making process in that a measured or observed laboratory test result from an individual is compared with reference interval for the purpose of making a medical decision, therapeutic management decision, or other physiological assessment.

How to interpret test results

- Reference ranges:

  derived from healthy young adults

  must minimize pre-analytical variables e.g. diet, stress, drug regimen, body habitus.

Reference ranges

- Ideally, the individuals should be selected from a reference population using specific criteria, including exclusion criteria (which might include recent surgery, tobacco use, over-the-counter medications, etc.) and partitioning criteria (which might include age,gender, race, etc.).

Reference ranges

Must consider the many variables that can affect laboratory tests in the elderly:

- composition of the body
- genetic influences
- geography and environmental temperature
- body habitus
- malnutrition and diet
- smoking, exercise, drugs

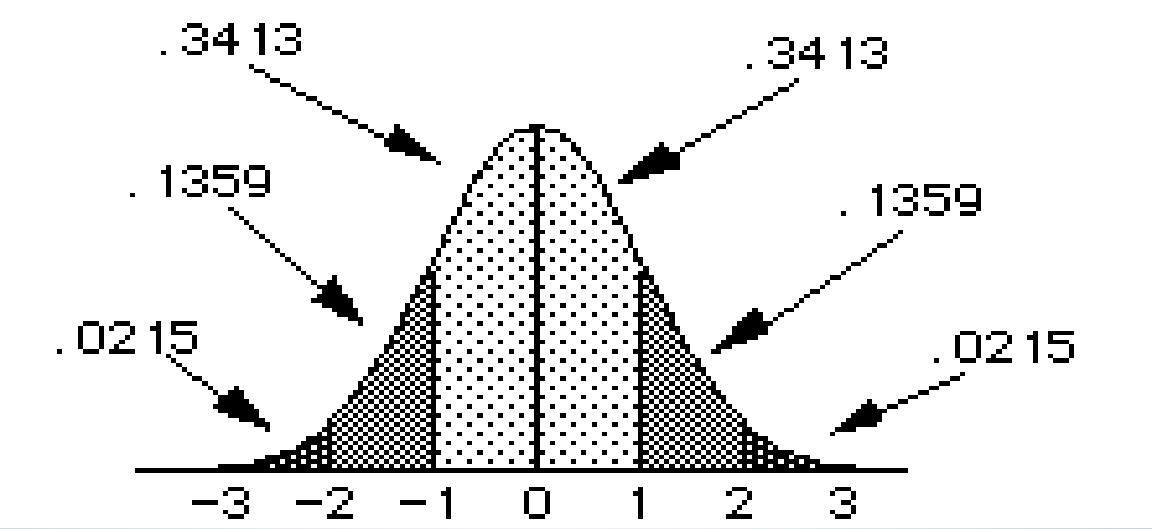
Reference ranges

- A multitude of RIs are available in the literature for persons greater than 65 years of age. Unfortunately no standardized method currently exists for selecting a reference population, or calculating RIs for this population. This in combination with poor reporting of methodologies, lack of confidence intervals for RI estimates and potential analytical variation makes it very difficult to consolidate findings and apply them to current situations.

Reference ranges

- If the distribution of the test results is Gaussian, a **parametric** method may be used. The reference range is defined as the mean plus or minus two standard deviations: Reference Range = $X \pm 2SD$

- Usual laboratory reference intervals are constructed in a way that defines 5% of people who are normal as lying outside the reference interval.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Aging

- Understand the effect of aging on different laboratory parameters to avoid the following pitfalls:

  clinically significant results could be dismissed as due to age.

  results normal for age could be considered pathological.

Physiology of aging

- "Normal aging refers to the common complex of diseases and impairments that characterize many of the elderly."
- Many physiological functions decline but normal decline is **not** considered disease.

Physiology of aging

- Body composition:↓ lean body mass, ↑adipose tissue.
- Nutritional requirements: identical to younger individuals with same level of activity.
- Glucose metabolism: ↑resistance to insulin.

Physiology of aging

- There are prominent changes in the structure and function of the **vasculature and the myocardium** in older adults when compared to younger adults. These changes are apparent even in the absence of risk factors other than age and in the absence of overt cardiovascular disease. However, these age-related alterations in the vasculature and the heart may render the cardiovascular system more susceptible to the detrimental effects of cardiovascular disease.

Physiology of aging

- there are both structural and functional changes in the **lungs** together with alterations in the control of breathing and more general immunologic alterations in the elderly. The changes are not just a direct consequence of age but are also affected by environmental exposure and coexistent comorbidities.

Physiology of aging

- **neurologic findings** of normal aging include subtle declines in cognitive function, mildly impaired motor function, and altered sensory perceptions. However, exaggerated impairments in cognitive, behavioral, motor, and sensory function suggest the onset of neurologic diseases that commonly afflict the older adult.

Physiology of aging

- The **gastrointestinal tract** generally maintains normal physiologic functioning in the elderly population. Most new GI symptoms in otherwise healthy older patients are due to pathology rather than to the aging process alone. These patients merit attentive and expeditious evaluation and management since their ability to tolerate illness is lower than that of younger patients.

Physiology of aging

- The **endocrine functions** that are essential to life, such as adrenal and thyroid functions, show an overall minimal change in basal levels with aging even though there are complex changes that do occur within the hypothalamo-pituitary-adrenal/thyroid axis.

Effects of aging

- Endocrine system: ⇓ T4 production but
  ⇓ elimination,
  ⇓ sex hormones, GH, DHEA-S,

Physiology of aging

- **Musculoskeletal problems**:

increased incidence of common musculoskeletal disorders in the elderly, such as rheumatoid arthritis and polymyalgia rheumatica. The high burden of musculoskeletal disease in elderly people also reflects the impact of the aging process on tissues which make up the musculoskeletal system, such as articular cartilage and bone.

Physiology of aging

- **Immune system**:↑ susceptibility to infection, autoimmune diseases, cancer.

Maladaptive response to antigens leading to the "syndrome of prolonged inflammatory response"

Reference ranges

- Greater than 60% of studies reported **increases** in:

alkaline phosphatase, creatinine, follicle-stimulating hormone, glucose, ϒ-glutamyltransferase, lactate dehydrogenase, low-density lipoprotein cholesterol, luteinizing hormone, magnesium, sex hormone binding globulin, thyroid-stimulating hormone and urea with age

Reference ranges

STUDY #1

- Greater than 60% of studies reported **decreases** in:

albumin, total bilirubin, total calcium, estradiol, insulin-like growth factor-I, iron, free and total testosterone, and vitamin B12 with age.

Reference ranges

- Analytes that were reported to **not change** with age in greater than 60% of studies include:

aspartate aminotransferase, chloride, high-density lipoprotein cholesterol, potassium, total protein, sodium and triglycerides. Conflicting results were reported for alanine aminotransferase, cholesterol, and creatine kinase.

Common analytes

Results from Geriatric Clinical Chemistry reference values:

- Electrolytes-Na, K, Cl, $CO_{2:}$

  similar from young adults to age 100

- Calcium-phosphate metabolism

  ionized and total calcium: variable reports, wider reference interval.

  phosphorus: slight decrease in men no change in women

Common analytes

- Glucose : increases from young adults to centenarians.

  Likely a pathological manifestation.

- Insulin: increases markedly in the 60-90 age range.

  Attributed to decreased muscle sensitivity and increased resistance.

Common analytes

- **Follow diagnostic criteria for DM of CDA and ADA:**

  random glucose:

  ≥ 11.1 mmol/L

  fasting glucose:

  ≥ 7.0 mmol/L

Common analytes

- AST, ALT:most report no changes.
- ALP: increased in ♀age 60-90 to reach levels seen in ♂.

  in ♂ no increase was seen.
- Due to post menopausal hormonal changes?

Common analytes

- ALP young women: 35-104 U/L

- ALP women age 60-90: 50-162 U/L

this increase in ALP in elderly women is frequently attributed to hormonal changes after menopause.

Common analytes

- GGT: contradictory reports, some show no change others an increase.
- CK: in both men and women there is a slight increase in the 60-70 year olds but a decrease at > 70 y.

Common analytes

- Urea: steady but modest increase in urea values in the 60-90-year olds.

  the decrease in renal function is thought to be due to a decrease in number of glomeruli and possibly a decrease in renal blood flow.

Common analytes

- Creatinine: concentrations were essentially unchanged between young adults and 60-90-y-olds.

  although there is decreased renal excretion of creatinine this is counteracted by a decrease in muscle mass.

Do not assume normal renal function

USE eGFR!!!!

Nutrition and aging

- Changes in body composition with aging:
  - ⇓ lean body mass
  - ⇓ intracellular water
  - ⇑ body fat

Malnutrition

- Can be difficult to define and diagnose malnutrition
- malnutrition represents the consequences of an insufficient intake of nutrients relative to the individual's needs.
- PEM is the form most often encountered in the elderly.

PEM

- Diagnosis of PEM:

  1. history and physical exam

  2. weight loss (> 10% in 6 months) and albumine < 30g/L.

  3. anemia, lymphocytopenia

  4. BMI < 21

PEM

- Laboratory tests affected by (PEM):
  - ⇓ albumine
  - ⇓ transferrin
  - ⇓ prealbumine
  - ⇓ Hg

Common analytes

- Proteins:

  Total protein: unchanged.

  Albumin: negligible decrease with age.

  Some report a slight ↓ in UL while the LL↓ is more significant.

  This could indicate effect of malnutrition.

Common annalytes

- Proteins:

  transthyretin (pre-albumin): means similar to young adults.

  transferrin: range, mean and median ↓ with age.

Common analytes

- Lipid profiles: reference ranges are not used instead we rely on “target values”.
- Global risk assessment applies to patients age 20-79 years. (Recommendations for the management and treatment of dyslipidemia).

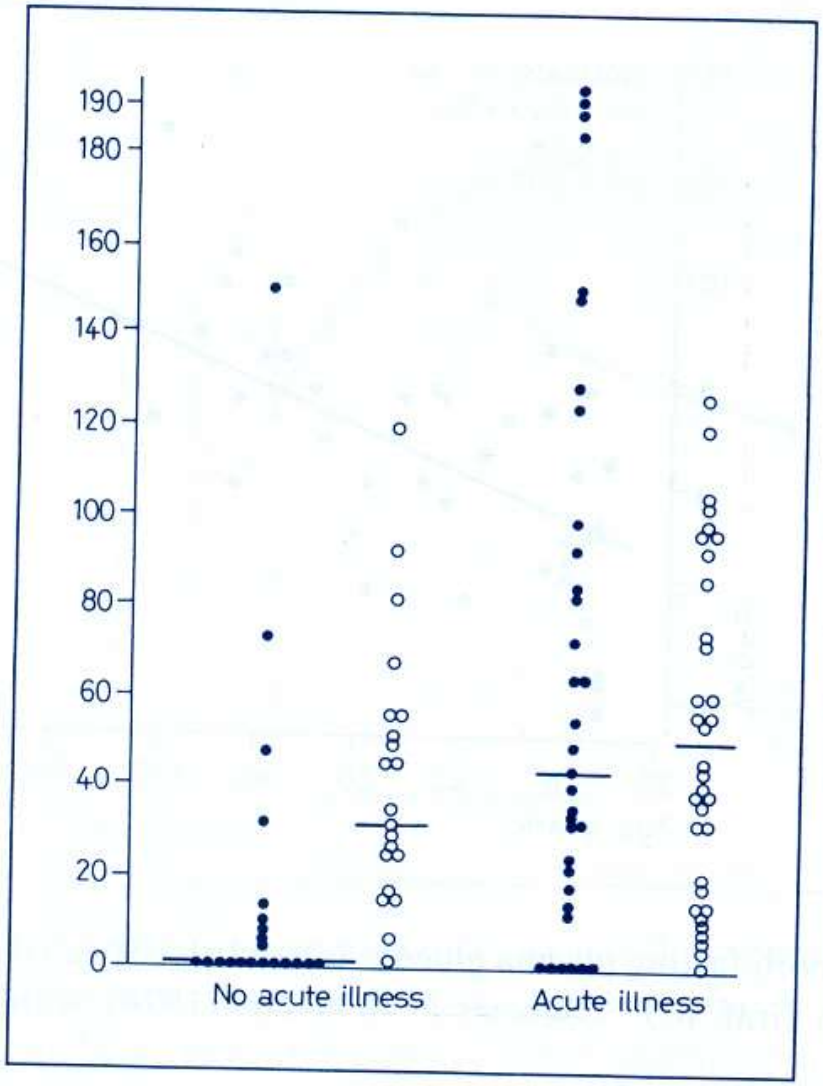
Common analytes

- Cholesterol levels in patients $\geq$ 90 years of age tend to decrease.
- Survival of the fittest?

Common analytes

- C-reactive protein: one study showed a median value of 1mg/L in the 25-34 y age group and a 2 mg/L value in the 65-74 y age group.
- ESR: values are higher in the elderly with values < 40 mm/h considered “normal”.

Serum C-reactive protein and erythrocyte sedimentation rate



Serum CRP concentration mg/l (●) and ESR mm/h (○) in individual patients on the morning after admission. From Kenny, R.A.; et al.: A comparison of the erythrocyte sedimentation rate and serum C-reactive protein concentration in elderly patients. Age Ageing *14:* 15–20 (1985), with permission.

Common analytes

- Hemoglobin: WHO considers values of

  < 130g/L in men

  < 120g/L in women

  clinically significant.
- No significant change with age.
- Other parameters of CBC show no significant change in healthy elderly patients.

Common analytes summary

- Unchanged values:

Potassium

Sodium

Calcium

Phosphorus

Magnesium(↓ but remains within RR)

- Unchanged values:

AST

ALT

GGT

Bilirubin

Common analytes summary

- Unchanged values

pH

pCO_2

Total protein

Creatinine

Serum folate

- Unchanged values

Hb

Hct

Platelets

WBC

Common analytes summary

- Increased values:

Lipid profil

Glucose

PSA

ESR

C-reactive protein

- Decreased values:

eGFR

Albumin

conclusion

- Abnormalities identified in haematological and biochemical testing are not due to age but to age-related illnesses.
- Therefore, when results outside the reference intervals are found, identification of disease states should be made.

- We would support the previous contention that intraindividual differences may be of greater validity in older populations rather than interpreting results within the context of reference intervals. (Ann Clin Biochem 2003; **40**: 274–279)

conclusion

- Lipid profile: rely on guidelines
- Alkaline phosphatase: ↑ RR 142 U/L
- Glucose: rely on CDA guidelines
- ESR: ↑ RR 40 mm/h

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