LABORATORIES AND GERIATRICS: MORE THAN REFERENCE INTERVALS

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INTRODUCTION

- Radical improvements in health care and general lifestyle have brought about longer life expectancy and, with it, a demographic phenomenon that has never been observed before.

- The steady growth of the proportion of older adults in the general population, especially in industrialized countries, has resulted in what is called an inverse demographic pyramid.

INTRODUCTION

- The subject of geriatric medicine has gained in popularity, among the:
  - Members of the professional community
  - General public
  - Laboratory medicine

- Except for an occasional call to adjust the reference intervals for specific tests, there has been no fundamental discussion of the consequences of the current demographic trend in the population—that is, until now.

OBJECTIVITY AS A BASIC PRINCIPLE OF IN VITRO DIAGNOSIS

- A biologic sample such as blood or urine collected from the patient would be analyzed for its physical and/or chemical properties, and the result would then be interpreted in terms of clinical information indicating the health status of the patient.

- If the procedure is properly calibrated, the results can be expressed quantitatively and described not in words, as is the case for other diagnostic disciplines, such as pathology or radiology, but as an exact numeric value.

BASIC PRINCIPLE

- The result of a laboratory analysis is not a descriptive observation derived from a subjective experience of the operator, but is an objective measurement, which always is related to a deductive postulated standard.

- Because most of the results provided by laboratory investigations can be considered as data that are generally reproducible and comparable, laboratory analysis represents a valid instrument of modern, evidence-based medicine.

BASIC PRINCIPLE

- To keep the clinical interpretation of these data objective, as much as possible, every numeric test result is usually completed by a reference interval, which is listed on the same line next to the test result value.

- The reference intervals have been derived from the standard statistical distribution of test results obtained from a demographic sample drawn from the normal adult population; normal is understood to be synonymous with healthy.

BASIC PRINCIPLE

- The statistical reference interval is based on the 95th percentile of Gaussian normal distribution (the bell curve).
- 5% of results obtained from healthy individuals will always be outside the reference range yet have no pathologic correlation.
- It follows that even in the case of a healthy individual, the probability that a ***random test result value*** would fall outside the reference interval proportionally increases with the number of the same laboratory tests performed on that same healthy individual.

BASIC PRINCIPLE

- Thus, ironically, the larger the number of tests undertaken, the higher the probability of a patient not being found normal, which shows that the statistically based reference concept has its limits.

- Every person is not just an anonymous member of a collective, but a unique unrepeatable individual.

GERIATRIC INDIVIDUALITY

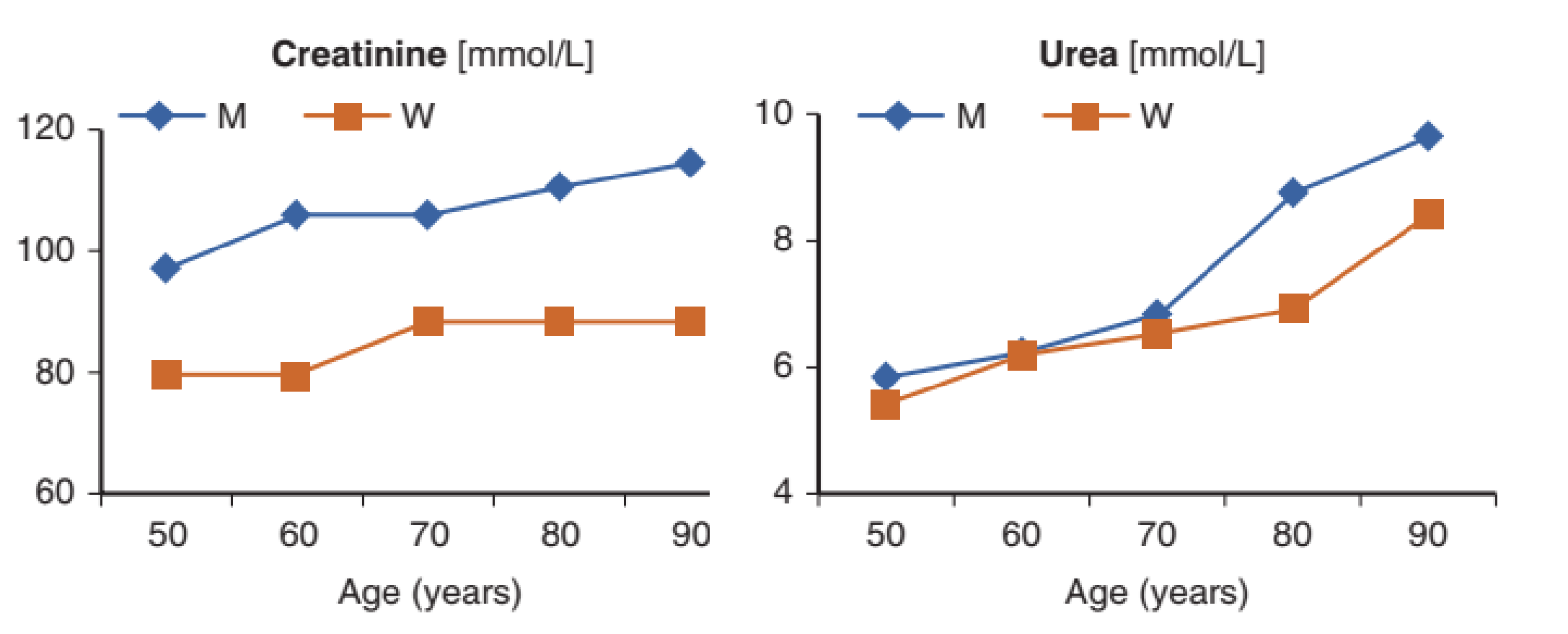
- From the point of view of the sociology, the answer to the question whether an older adult is healthy or sick can neither be based on actual performance at work nor reduced to the fact of whether he or she has secured a physician's note from the employer.
- By contrast, in ***older adults***, more than in younger adults, the difference between being healthy or sick is based on a very subjective feeling reflecting the quality of one's life.

- However, there is yet another aspect to be considered in geriatric laboratory medicine. It is the continuous progressive decline of physiologic functions in an ***aging*** human body.

GERIATRIC INDIVIDUALITY

- Age-dependent impairment of renal and pulmonic functions, progression of osteoporosis, a decrease of various endocrine functions, and general weakening of immunity at an older age are typical examples.
- Attempts to establish age-related reference intervals, similar to those used in pediatrics, have proven to be **unsuccessful**.
- Such intentions **failed** because the approach did not and could not address the individuality and variability of the senescent process from the ***clinical*** and ***biologic*** point of view for each patient.

CORRELATION OF DIFFERENT LABORATORY PARAMETERS WITH AGE



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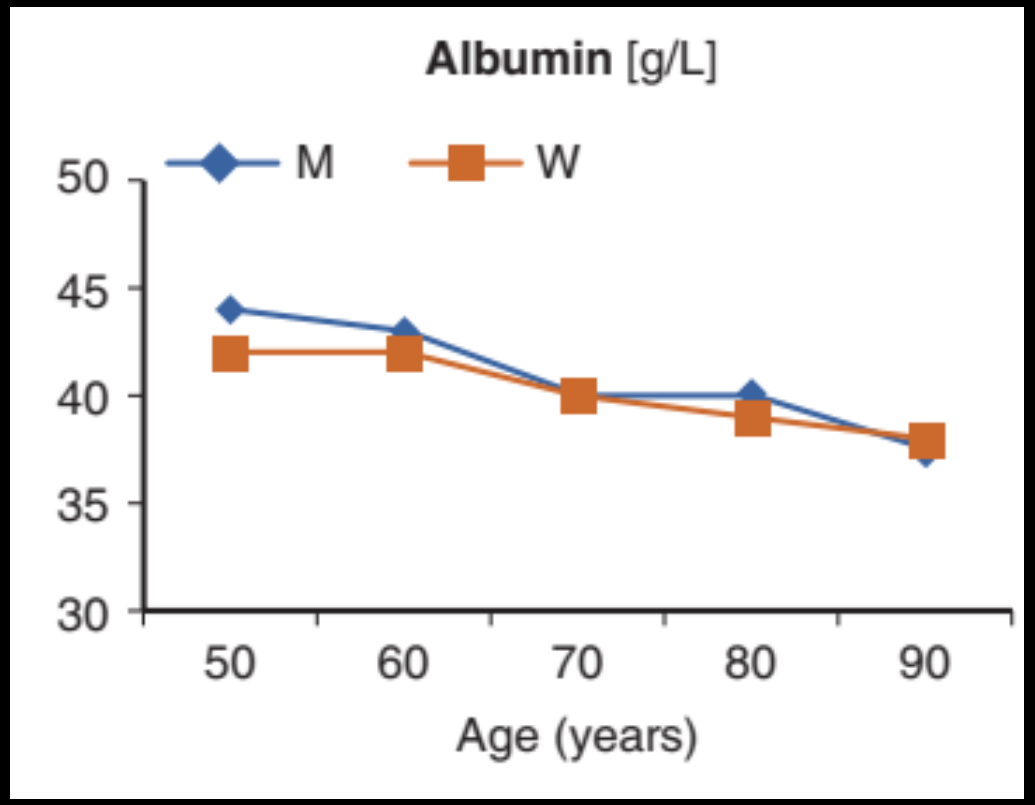

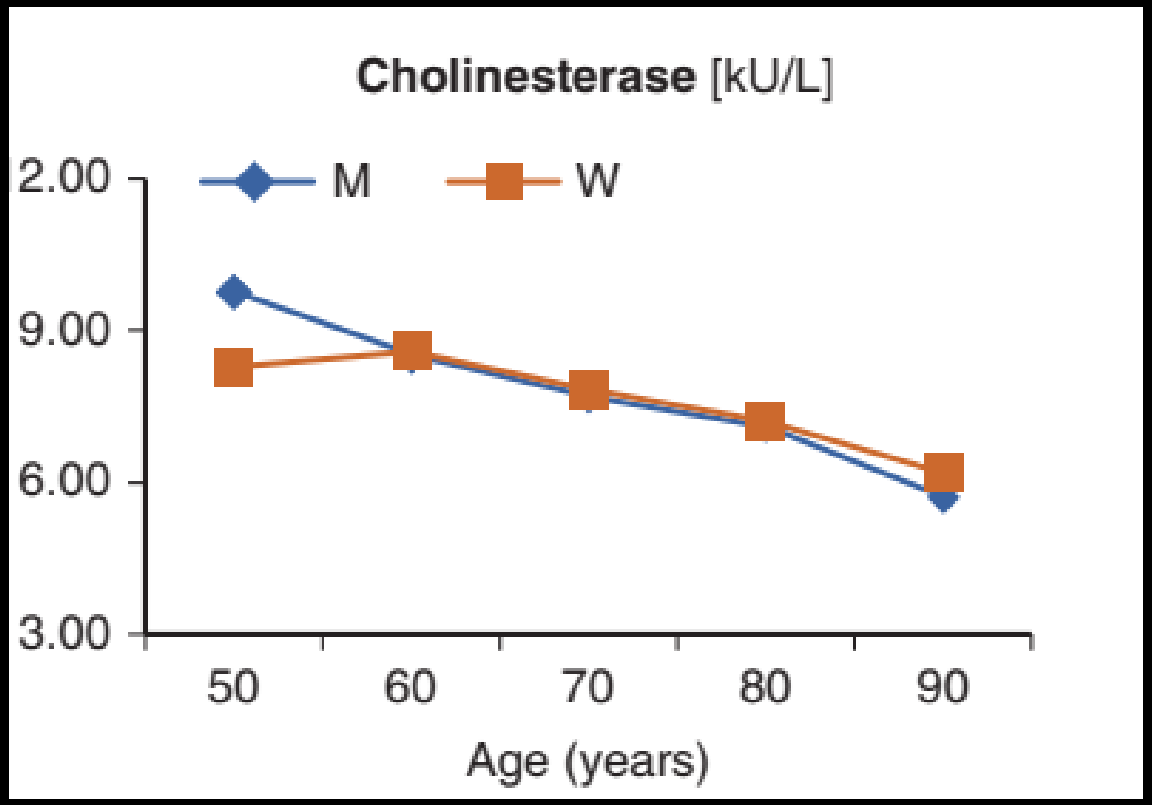

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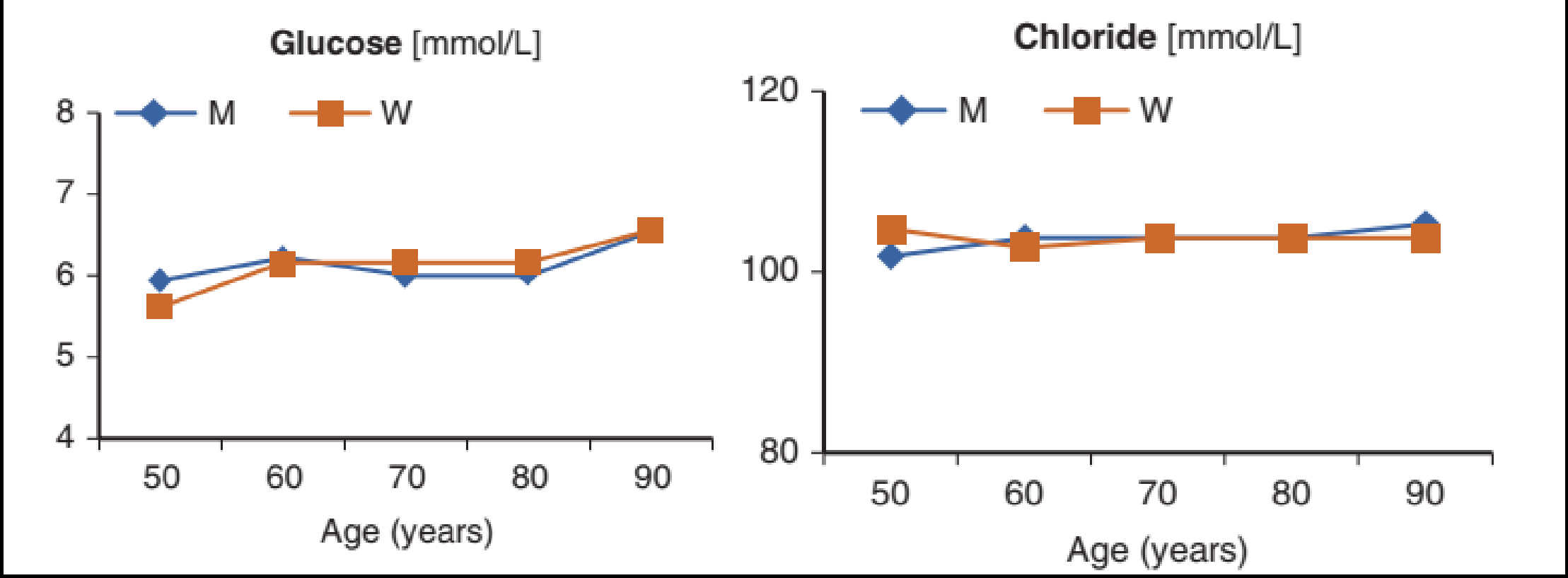

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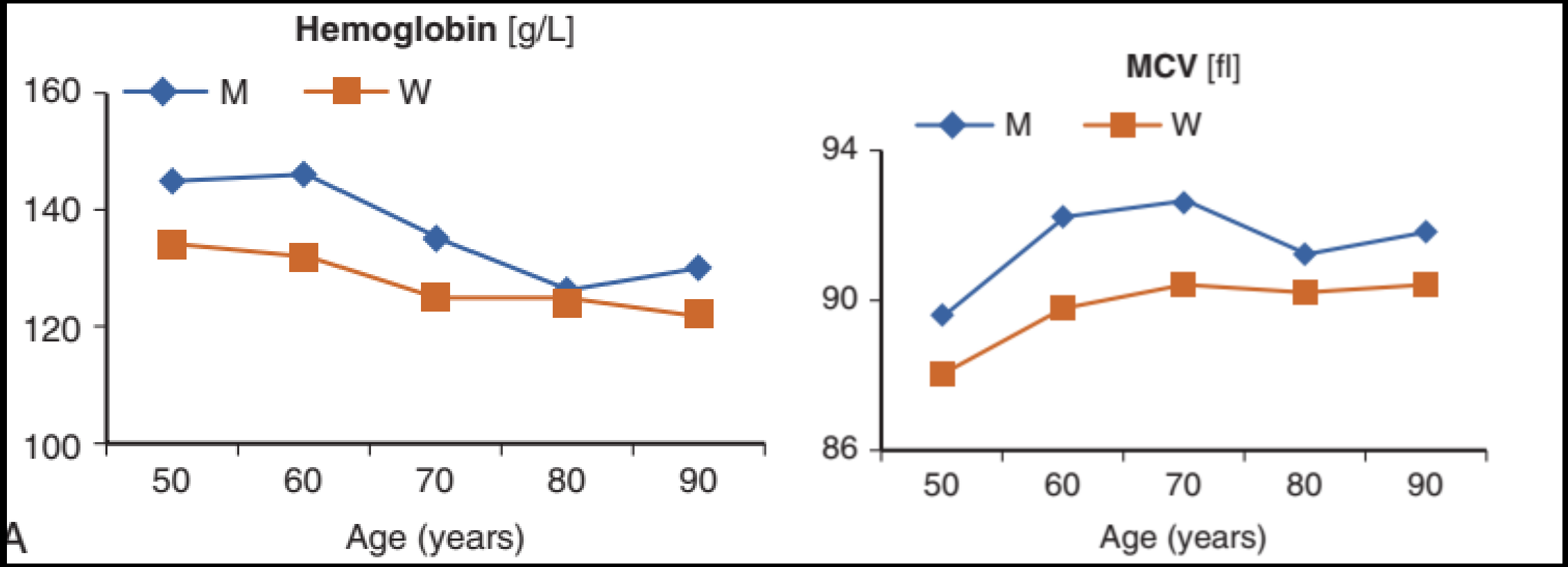


GERIATRIC INDIVIDUALITY

- In pediatrics, as well as in the adult medicine, most of the population is healthy, and those who are sick usually have only one cause (rarely more than one) for their illness.
- The primary aim of **pediatric** and adult medicine is to detect and cure the disease as efficiently as possible to protect the future life chances of the patients.
- **Adult** medicine strives to **return** adult patients to their normal productive (working) life as quickly as possible.
- Geriatrics is different.

GERIATRIC INDIVIDUALITY

- Here, the clinical histories of older adults who have reached the last part of their lives are much more complex than those in the previous stages of their life.
- Not only **Past** crises and emergency situations, but also periods of prosperity and affluence—perceived as the good times—all have influenced the actual health state of an older adult.
- Diseases and trauma, which randomly occur in the course of life and have left more or less relevant after effects and physical and emotional scars in all of us, **contribute** to the **specificity** of the clinical status of each **older adult**.

GERIATRIC INDIVIDUALITY

- Moreover, with **advancing age**, the probability of manifestation of genetically or secondarily predisposed diseases **increases** progressively.
- To describe all these inputs, clinical geriatrics uses the term *multimorbidity*.
- It is a **very important** term because it characterizes the occurrence of several diseases and/or pathologic processes to which an older patient is subjected, often in **oligo-symptomatic** and **atypical ways**.

GERIATRIC INDIVIDUALITY

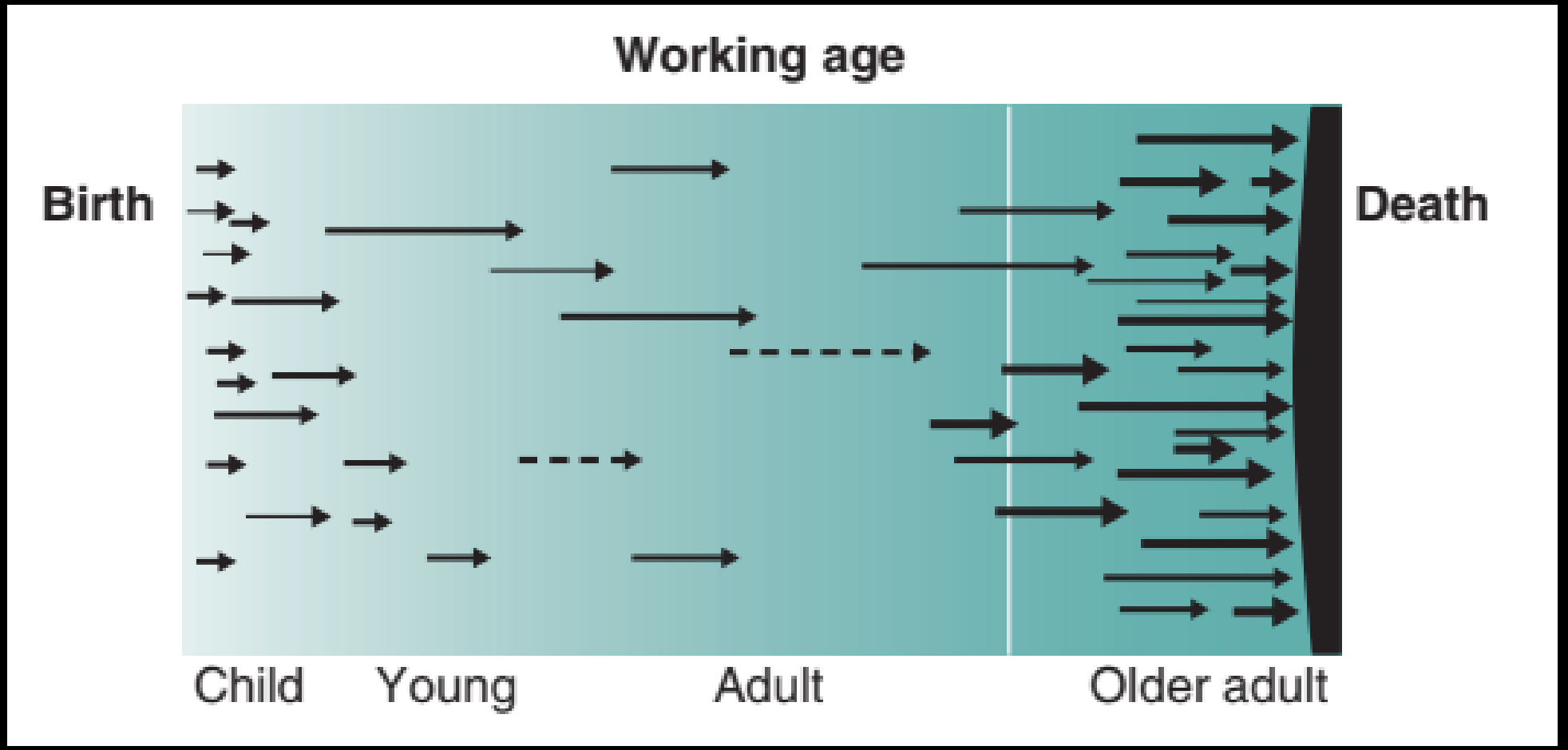
- Many different involute processes can be considered as typical physiologic processes of older age.
- They all can occur with individual accentuation and can be **triggered** by different random events at different moments of the life.
- In this context, it becomes more and more difficult to define unequivocally the meaning of the term *biologic age*.

GERIATRIC INDIVIDUALITY

- Finally, one has to accept that **death** itself is often a **result** of **one or more diseases** breaking out during the ultimate period of life.

- To sum up, when speaking about the normality of patients in geriatrics, it has to be kept in mind that an older, perfectly healthy individual is a **biological rarity**, rather than a *normal case*.

AGE AND DISEASES EFFECTS



MONITORING IN GERIATRICS

- One of the actual trends of today's laboratory medicine is the consolidation of laboratories, which has been imposed on the existing laboratory community by the markedly improved efficiency of laboratory testing as a whole.
- Usually, this means the concentration of medical laboratories in large, semi-industrial diagnostic institutions, a hub to which the work is outsourced.
- The separation of laboratory medicine from clinical institutions has brought about the depersonalization of the communication between clinicians and laboratory specialists.

MONITORING IN GERIATRICS

- Consequently, certain aspects, which have theoretically been known to affect the diagnostic significance of laboratory testing, have gained an unexpected actuality. One of these concerns the pre-analytic studies.

- Such pre-analytic conditions include:
  1. orthostatic effects (especially in patients with edema),
  2. effects related to impaired mobility,
  3. effects related to nutritional status,
  4. effects related to seasonal influences.

MONITORING IN GERIATRICS

- Because of impairment of the functionality of different organs (e.g., liver, kidney, lung, immune system) in older adults, minor pathologic influences will be **compensated** for with **less elasticity**. This, in turn, is reflected by the **higher variability** of laboratory results.
- Moreover, the poor venous status of some older patients can cause difficulties in regard to **phlebotomy** and **blood collection**, which are then responsible for hemolytic sera and inadequate sample volumes that might be too small for an optimal analytic process.

MONITORING IN GERIATRICS

- The fact that the sheer number of samples sent to the laboratory by geriatric practitioners can be far less than those that originate, for example, in the intensive care unit, can lead to **negligence** and **sloppiness**.

- This can result in geriatric samples being treated with less interest and therefore given the lowest priority.

MONITORING IN GERIATRICS

- Well known are situations when, in a nursing home, the collected samples are **ignored** by the courier and left behind on the counter for a later batch in the day or even for the next day's collection.
- The increased turnaround time is always disadvantageous, whether because of the **stability** of the analytic (substance, enzymatic activity, or other subject of chemical analysis) or the actual diagnostic information to be submitted for review by the attending physician.

MEDICAL SIGNIFICANCE OF LABORATORY RESULTS IN OLDER ADULTS

Possible Clinically Significant Alterations of Laboratory Parameters Used for Older Adults		
Parameter	**Usual Significance in Adults**	**Possible Alternative Significance in Older Adults**
Blood urea nitrogen	Renal insufficiency	Acute catabolism (often reversible)
Albumin	Renal or hepatic insufficiency	Biologic age, malnutrition, frailty
Cholesterol	Risk of atherosclerosis (high cholesterol)	Malnutrition, marker of fatal prognosis (low cholesterol)
γ-Glutamyl transpeptidase	Alcoholism, cholestasis, hepatitis	Liver congestion (due to heart insufficiency)
Amylase	Pancreatitis	Parotitis (often during summer season); macroamylase
Lactate dehydrogenase	Parenchymal damages, hemolysis	Phlebotomy problem

MEDICAL SIGNIFICANCE OF LABORATORY RESULTS IN OLDER ADULTS

Possible Clinically Significant Alterations of Laboratory Parameters Used for Older Adults		
Parameter	**Usual Significance in Adults**	**Possible Alternative Significance in Older Adults**
Total protein	Chronic inflammation	Exsiccation, myeloma
C-reactive protein	Inflammation, acute phase	Infection, necrosis (sometimes unique conclusive marker)
Erythrocyte sedimentation rate	Chronic inflammation	Occult neoplasm
Partial thromboplastin time	Heparin, hemophilia	Lupus inhibitor
Hemoglobin	Bleeding	Anemia of older adults, myelodysplastic syndrome
Mean corpuscular volume	Alcohol abuse	Deficiency of vitamin B12 or folic acid

CHOLESTEROL

- Usually, the mean level of cholesterol in serum correlates with the cardiovascular risk, which **increases with age**.
- However, starting from the sixth decade of life, this increase stops, and cholesterol levels begin to **decrease**. Such behavior can be explained by the successive demographic change of the cohort.
- At the same time, cholesterol has also became a marker for nutritional status because its decrease correlates with malnutrition.
- Finally, at the end of this age dependent correlation, the sudden decrease of the cholesterol level may indicate a **worsening life expectancy prognosis**.

BIAS FACTORS

- Due to symptomatic, supportive, and palliative therapy, which is more important in geriatrics than in adult medicine, the geriatrician is sometimes forced to undergo therapeutic compromises—for example, using **corticosteroids** in patients with diabetes mellitus.
- In this situation, to optimize the individual therapeutic strategy, it is not enough to monitor clinical status. It is more important is to estimate the **still remaining functional** capacity of different **organs** and **systems**.

PROGNOSTIC INFORMATION

- In other words, parameters that enable the estimation of still remaining functional capacity and/or parameters that provide prognostic information are of particular importance in older adults.
- A good example of such an **important parameter** is the amount of brain natriuretic peptide (BNP) in the patient's blood because it provides quantitative information about the **degree of cardiac insufficiency** as it relates to congestive heart failure.

MULTIMORBIDITY

- Another important feature of geriatrics is the frequent presence of multimorbidity.
- In this context, Fair weather and Campbell have demonstrated that in **older adults**, "failing to make diagnosis when the disease is present or making a diagnosis when a disease is not present is likely to occur **twice** as often as in younger patients."
- In the same way, an autopsy study has shown that the **accuracy** rate of the **clinical diagnosis** of the immediate cause of death is no higher than roughly 50%.

MULTIMORBIDITY

- In this sense, it is meaningful to differentiate between multipathology and multicausality.
- Because multipathology can be seen as a complex of several impairments of the organism, the term *multicausality* is a more complicated one.
- It characterizes several dynamic pathologic processes, often convoluted in each other.

ATYPICAL SYMPTOMS, SIGNS, AND PATHOLOGY

- Often, pathologic conditions such as infections, cardiovascular diseases, acute abdomen, hyperthyroidism, and depression occur in older adults in an atypical and nonspecific way and with correspondingly atypical symptoms, physical findings, and laboratory results.
- However, the adequate estimation of **multiple** causative factors that are contributing to the current status of the patient can be more difficult.

MULTICAUSALITY

- Frequently, due to the propensity to think in terms of a single disease, it **can be difficult** for the clinician to decide which of the actual factors are important and will benefit the patient if treated.
- At the same time, the underestimation of multicausality, together with the progressive **decline** of the cognitive and physical status of the patient, can aggravate the problem of degradation of the diagnostic information.

THERAPEUTIC INTERVENTION OR CARING

- However, especially in view of the **prognosis** of the patient, there can be a discrepancy between the necessity of a diagnostic and therapeutic intervention on one side and the need for caring for a patient with appropriated dignity on the other side.
- In this case, even laboratory medicine faces ethical limits.

CONCLUSION

- With the growing proportion of older adults in industrialized countries, the role of **geriatric medicine** will grow accordingly.
- The trend will, in turn, create corresponding requirements for **better** efficiency in **laboratory diagnoses**.
- It is imperative to distinguish between geriatric medicine, which deals with the **wide variety of individuals** rather than samples, collectives, or groups of people, common in classic medicine.

CONCLUSION

- It is to be expected that soon geriatric laboratory medicine will be subjected to a **radical change of paradigms**.
- Not only the statistically revealed evidence, as obtained from studies of a large number of individuals, but also consideration of the individual patient, with his or her clinical individuality, status, predispositions, physiologic reserves, and prognosis, will need a thorough, in-depth review.

CONCLUSION

- It will not be sufficient to consider health solely from the deterministic point of view, observing differences between physiology and pathology of the **laboratory findings**.
- Similarly, it will be important to consider clinical individuality as a relative risk in the dimension of time for the rest of the patient's life.

CONCLUSION

- From the practical point of view, it would be necessary to pay more attention to limits of the diagnostic significance of laboratory testing of older adults.
- This should be considered especially for education programs for specialists in geriatric medicine.
- Research in geriatrics should concentrate on new diagnostic parameters that would enable a better estimation of the clinical risk to the patients.

Question