Clinical laboratory values in the aging population

NW Tietz, DF Shuey, DR Wekstein

Department of Pathology and Laboratory Medicine and Sanders-Brown Center on Aging, University of Kentucky Medical Center, Lexington KY 40536-0084 USA

Abstract: Over the last decades the average life expectancy of the human race has increased significantly; however, little change has occurred in the maximum lifespan. Of greatest interest, however, is the functional lifespan. In this context, the clinical laboratory can play an important role by (a) defining proper reference ranges, (b) identifying disease processes early, and (c) aiding in the treatment process. We report on the study of laboratory values in the aging between 60 and 90 y, and those >90 y of age. Electrolytes (Na, K, Cl, CO_2) are remarkably stable and deviate from the values in the young adults only in the very old (>90 y). Total calcium and albumin values decrease, while ionized calcium shows little change. Phosphorus values decrease in males but only marginally in females. Serum urea nitrogen increases, especially in the >90-y-old, while creatinine remains unchanged due to the progressive decrease in muscle mass. Osmolality values increase. Prealbumin, albumin and transferrin increase, while α_1-antitrypsin, retinol-binding protein and haptoglobin increase. Increases in glucose are accompanied by increases in insulin and C-peptide, except in the very old where the last two decrease. Total and HDL-cholesterol increase; however, cholesterol in the very old is similar to that in young adults. T_4, T_3, thyroxine-binding globulin, testosterone, estrogens and progesterone decrease, but prolactin, luteinizing hormone and FSH increase sharply.

Since antiquity the human race has had the desire to live a long life. Over the last few decades, there has been a significant increase in the average life expectancy due to a decrease in infant mortality and fatal diseases such as cardiovascular disease and cancer. In the USA, for example, the life expectancy has increased during this century from 47 to about 75 y. However, it is believed that we are approaching a maximum mean life expectancy. Even if we succeed in the elimination of all diseases that are the main contributors to death, the theoretical limit has been calculated to be 85 y ± an SD of 7 y. The observed increase in life expectancy will have a major impact on the world population. By the year 2020, the increase in the aging population is expected to be 159% in less-developed countries, 59% in developed countries and 69% in the USA. By 2050 the number of people >65 y world wide will be at least 2.5 billion. As a result, the traditional growth pyramid will soon be inverted with a narrow base and a broad tip.

The spectrum of life expectancies in various countries of the world is wide, ranging from 41 y in Afghanistan to 75 and 82 y, respectively, for males and females in Japan. Women of all races live longer than men. For males, the higher mortality begins in the womb; the ratio of stillbirths for males:females is 1.4:1.

The maximum lifespan of the human species (the lifespan of the longest lived individual for whom credible records exist) is 120 y. However, most important is the "functional lifespan," the period of healthy, productive life. In this context, the clinical laboratory can play a major role by defining proper reference intervals for the aging population by detecting disease processes early and by aiding in the treatment process. Our study of laboratory values in the aging extended over several years and included "fit" volunteers in the age groups of 60-90 y and >90 y of age. Selection criteria are described in detail in a previous communication which also contains more detailed data tabulations (see footnote).[†]

Electrolytes. The range of *sodium* values in the 60- to 90-y age group is surprisingly similar to that in young adults. In the >90-y population, the range widens slightly to 132-146 mmol/L. *Potassium* values in all age groups changed little; there was a slight extension of the upper range to 5.4 mmol/L. The *chloride* range is similar to that in young adults, but mean and median are slightly higher. Total CO_2 values increased slightly with age, possibly due to the decrease in diffusing capacity of the lung and increase in the rigidity of the thorax. *Total calcium* values tend to increase in the 60- to 90-y-old, but decrease in the >90-y age group. These decreases appear to be caused by decreases in serum albumin. In contrast, *ionized calcium* values show minimal increases in the 60- to 90-y population and a widening of the range in the >90-y-old. Increases are paralleled by increases in *parathyroid hormone (parathyrin; PTH)*. *Phosphorus* values decrease in the aging male, but only minimal changes are observed in females.

Renal glomerular filtration decreases with age as a result of 30-40% loss of glomeruli at age 80 y as well as decreased blood flow due to vascular changes and decreased heart output. These changes are accompanied by an increase in *urea nitrogen*, which is especially marked in the >90-y-old. In contrast, *creatinine* values show little change due to the concomitant decrease in muscle mass and associated decrease in creatinine production.

Uric acid values are said to increase with age, but we saw significant changes only in females. *Plasma osmolality* increases slightly with age -- a change that is paralleled by a decrease in body water content.

Proteins. Although changes in total proteins are minimal, significant changes have been observed in some individual proteins. Marked decreases occur in *prealbumin, albumin* and *transferrin*; all three proteins are clinically used as nutritional markers. On the other hand, the acute-phase reactants *retinol-binding protein*, α_1*-antitrypsin* and *haptoglobin* increase markedly with age. The upper range for γ*-globulin* increases slightly, and the range of *ceruloplasmin* narrows with age.

Glucose Metabolism. *Serum glucose* values increased with progressing age, but surprisingly *insulin* and *C-peptide* increase also until >90 y of age, when a marked drop is observed. These findings suggest that the initial increase in glucose is not caused by decreased endocrine function, but possibly by insulin resistance or decreased insulin receptors. Only in the very old does pancreatic endocrine function decrease.

Lipids. *Triglycerides* increase with age in both sexes, but values are very variable. *Total cholesterol* concentrations increase as well, but more in females than in males. However, values in volunteers >90 y old are at or even below the values found in young adults. *HDL cholesterol* is higher in the aging than in young adults, and values in females are higher than those in males.

Liver Function. *Bilirubin* values decrease most likely due to a decrease in muscle mass (and therefore heme), and decrease in blood hemoglobin content. Both result in a decrease in bilirubin production. *Aspartate aminotransferase (AST)* values change little, while *alanine aminotransferase (ALT)* shows a slight decrease. *Lactate dehydrogenase (LH)* is stable until 90 y but then increases markedly. LD isoenzymes change little with age except for LD-5 which decreases in the very old. γ *-Glutamyltransferase*

(GGT) values are higher in the elderly male and female. *Alkaline phosphatase (ALP)* increases steadily in females beginning with menopause; however, we have not observed similar increases in males despite reports in the literature to the contrary.

Muscle Enzymes. *Creatine kinase (CK)* values change little between 60 and 70 y of age, but decrease markedly in the higher age ranges of both sexes. Very marked decreases are seen in the >90 y old. *The CK-MB isoenzyme* also decreases with age and reaches undetectable values above 90 y. The observed decreases are due to a decreased muscle mass in general, but also to the 40-60% decrease in CK content of muscle tissue of the aging.

Pancreatic Enzymes. The enzymes *lipase, amylase* and *trypsin* increase especially in the >90 y old. Very marked increases are seen in some individuals without any signs or symptoms of acute pancreatitis. It has been speculated that these increases may be due to damage to the external surface of the acinar membrane or the basement membrane. Decreased renal function may also contribute to increases in these enzymes since amylase and trypsin (but not lipase) are excreted by the kidneys.

Immunoglobulins. *IgG* and *IgA* values increase with age, but *IgM* concentrations tend to decrease. *IgE* values are nearly identical to those in young adults, but in the aging we observed less outliers due to allergic reactions to specific allergens.

Thyroid function. The upper range for *thyroxine* decreases with age parallel with the decrease in the upper range of *thyroxin-binding globulin*. Values for *triiodothyronine (T$_3$)* decreased markedly, especially in the very old. It is not certain whether this decrease in due to decreased conversion of T$_4$ to T$_3$ in the peripheral tissues, or due to the possible presence of subclinical diseases. The decrease in T$_4$ and T$_3$ is accompanied by a decrease in the metabolic rate in the aging. *Thyroid-stimulating hormone (thyrotropin; TSH)* increases with age, but values in the >90 y old are close to those in young adults.

Pituitary Hormones. Pronounced increases were observed for *prolactin*, especially in females and volunteers >90 y old. *Lutropin (LH)* shows higher values in both sexes, and *follicle-stimulating hormone (FSH)* increases markedly in males as well as in females. *Corticotropin (ACTH)* values are close to those in young adults.

Sex Hormones and Adrenal Hormones. *Estrogens*, as well as *free, bioactive and total testosterone* values decrease. Testosterone values, however, were very variable, and some older volunteers had values similar to those in young adults. The decrease in testosterone is accompanied by decreased testicular function. Decreases also occur in *dehydroepiandrosterone, androstenedione* and *progesterone*. Essentially no changes were observed for *cortisol*.

Hematological Data. *Total erythrocyte, leukocyte* and *platelet* counts are lower in the aging population. The low reference point for *hemoglobin* increases, but no change was observed in the upper range. *Serum iron* values are lower in the aging of both sexes.

Further studies to confirm reference intervals in the aging are required. It also needs to be evaluated whether or not statistically significant differences in laboratory values in the aging population also have clinical significance, and if they are the result of a normal aging process, subclinical disease, or nutritional factors.