

## CLINICAL IMPLICATIONS OF GLUCOSE TOLERANCE TEST INTERPRETATION IN RELATION TO THE AGE OF THE SUBJECT

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**Summary.** Based on data from personal and field literature on senescence and its possible relationship with the decreased glucose tolerance, the authors discuss the interpretation of glucose tolerance test. Arguments are gathered to support a methodology aimed at standardizing the dosings and the interpretation of the results. Mention is also made of the possible implications of enzyme and radio-immune dosings in explaining metabolic peculiarities with advanced age.

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The paper includes essential data on the discovery of diabetes mellitus in the aged. Previous studies (1969) pointed out the increase in fasting glucose levels with each advancing age decade as follows:

| Age of subject (years) | Fasting glucose levels (mg%) |
|------------------------|------------------------------|
| 20-29                  | 112                          |
| 30-39                  | 118                          |
| 40-59                  | 125                          |
| over 60                | 130                          |

(according to Honigmann and coll. - 1969)

According to West K. M. fasting glucose levels over 100-110 mg % occur in a small number of aged persons [29]. Verifying the changes in glucose levels in relation to advancing age and based on fasting glucose test and on GTT, Nițulescu J., Ornstein L., Sibi Maria [26] found insignificant variations against standard glucose levels in young persons. Mention should be made that the data were not statistically analysed, their significance being estimated per cent. The topic has been taken over by the authors of this paper [15] and fasting glucose levels as well as GTT were calculated based on Student Fischer test on aged subjects. The dynamic checking of glucose tolerance yielded results comparable with those obtained by Nițulescu, Ornstein, Sibi; GTT curves revealed certain peculiarities related to the context habits, in the first place. Neither does our research infer the necessity for special standards with the aged. According to Pyke D. A. (quoted by [25]), the general metabolic disturbance would account for the elevated glucose levels in the aged. The factors inducing decreased glucose tolerance could be: tissue wear off, decrease in number and functional capacity of beta cells.

According to Harth A. [13], the diagnosis of diabetes mellitus is positive in all the aged persons with fasting glucose levels exceeding 130 mg % (and no glycosuria). The senile hyperthyroidism which can not be discovered clinically, could favor hyperglycemia and glycosuria.

In order to discuss the diagnosis in relation to glucose values during GTT, we shall first give the data reported by Honigmann and coll. (1969).

Table 1

| Age<br>(years) | Minutes                      |                              |                              |
|----------------|------------------------------|------------------------------|------------------------------|
|                | 30                           | 60                           | 120                          |
| 20-29          | 155-175 mg $\%$ <sub>0</sub> | 145-176 mg $\%$ <sub>0</sub> | 105-125 mg $\%$ <sub>0</sub> |
| 30-39          | 170-190 mg $\%$ <sub>0</sub> | 155-185 mg $\%$ <sub>0</sub> | 105-125 mg $\%$ <sub>0</sub> |
| 40-49          | 185-210 mg $\%$ <sub>0</sub> | 165-200 mg $\%$ <sub>0</sub> | 105-125 mg $\%$ <sub>0</sub> |
| 50-59          | 185-210 mg $\%$ <sub>0</sub> | 185-215 mg $\%$ <sub>0</sub> | 105-125 mg $\%$ <sub>0</sub> |
| 60-69          | 185-210 mg $\%$ <sub>0</sub> | 195-230 mg $\%$ <sub>0</sub> | 105-125 mg $\%$ <sub>0</sub> |
| 70-79          | 185-210 mg $\%$ <sub>0</sub> | 195-230 mg $\%$ <sub>0</sub> | 130-160 mg $\%$ <sub>0</sub> |

(according to Honigmann and coll. - 1969)

Referred to fasting glucose values, the variation of the figures does not allow a distinction between 'diabetic' and 'normal' persons. According to Mana and Tchobrotsky [21] diabetes mellitus could be suspected when fasting glucose values exceed 1.30 g $\%$ <sub>00</sub> (capillary blood) and 1.25 g $\%$ <sub>00</sub> (venous blood). The values close to the above-mentioned ones require an interpretation within the clinical context which is the more difficult as the subject is older. Joshu's criteria of the diagnosis of diabetes mellitus in the aged are the following: glucose levels exceeding 13 mg $\%$ , with glycosuria, or glycosuria exclusively (the renal threshold is usually higher in the aged). Diagnosis is rendered more difficult by the uptake of glucose due to the delayed, weaker reaction of the glycoregulatory system in the aged. According to Köbberling J. A. and coll. [20] glucose levels indicating the disease are: GTT 200 mg $\%$  at one hour and 150 mg $\%$  at 2 hours. The above-mentioned authors consider that 170 mg $\%$  at one hour and 130 mg $\%$  at 2 hours do not indicate diabetes mellitus. For diagnosing diabetes mellitus the following paraclinical parameters should be used:

Table 2

|                        | Absent clinical signs |              |              |
|------------------------|-----------------------|--------------|--------------|
|                        | increased             | increased    | normal       |
| Fasting glucose levels | +                     | -            | +            |
| Glycosuria             | +                     | -            | +            |
| GTT                    | pathological          | pathological | pathological |

(according to Mana H., Tchobrotsky G., 1968)

Glycosuria is frequently absent in the aged, even when fasting glucose levels have increased; as a peculiarity of diabetes mellitus in the aged, the diminution or even normalization of glucose levels have been noticed to accompany the onset of complications [7, 8]. The frequent glycoregulatory disturbances in coronary patients with overt diabetes mellitus [3, 4, 5] raise certain difficulties of diagnosis.



The interpretation of GTT curves has always been a problem with the aged outside the clinical context of diabetes mellitus disease [6, 15]. As glycosuria is sometimes absent, even with elevated glucose levels reaching  $3 \text{ g } \frac{\text{g}}{100}$ , polyuria and polydipsia are also absent, making the diagnosis of diabetes mellitus even more difficult in these cases [1, 19]. The possibility of diabetes mellitus with normal fasting glucose levels requires the use of the glucose uptake test — carried out with 50–100 g glucose *per os* (generally 1 g/kg body weight). Some authors consider the aged a virtual diabetic. According to Graff E. S. and coll. [11], the higher incidence of latent diabetes in advanced ages is statistically significant; the data are based on the fact that a certain number of persons with normal oral GTT when young, later presented either latent or clinically overt diabetes; these authors suggested a genetic proneness to diabetes to account for the above-mentioned fact.

Because no standard norms have been established for persons aged over 40–50, the suggestion has been advanced to consider normal glucose values those resulted from adding an average amount of  $0.10 \text{ g } \frac{\text{g}}{100}$  glucose to each age decade.

Table 3

| Author                 | Year | to add $\frac{\text{g}}{100}$ | Age decade                 |
|------------------------|------|-------------------------------|----------------------------|
| Mana-Tehobrontsky [21] | 1964 | 0.10–0.12                     | to each age decade over 45 |
| Mana-Tehobrontsky [21] | 1965 | 0.13                          | to each age decade over 50 |
| Fajans-Conn [9]        | 1965 | 0.10                          | to each age decade over 40 |
| Ricketts et al [28]    | 1966 | 0.10–0.15                     | to each age decade over 30 |

(fasting glucose values resulted from the increase in glucose amounts according to the table)

Mention should be made of the National Health Survey (1960–1962) carried out on 111,000 GTT curves, with 50 g glucose; they pointed out a linear increase by 14 mg % with each age-decade (quoted by [24]). With 100 g glucose, — a study conducted at Tecumseh (Michigan) — the elevation of the venous blood glucose levels in 4,000 persons was also linear and progressive: 100 mg % (16–19 years) and 177 mg % (70–79 years); the increase was thus 13 mg % by age-decade, which is not a significant difference from the GTT curves yielded by 50 g glucose [14]. Butterfield's study conducted on a London community which received 50 g glucose *per os* measured capillary blood glucose levels (the values were thus found to increase by 14 mg % and 7 mg % at 1 and 2 hours, respectively, by age-decade (quoted by [25])). The epidemiologic studies carried out by Mineu and coll. between 1970–1972 aimed at establishing the limits of the normal glucose levels in relation to age, 2 hours after the intake of 100 g glucose, as follows: 122 mg % (25–30 years), 145 mg % (over 60–65 years). Glucose uptake and cortisone stimulation in the aged are considered useful only for research goals [27], which also require enzyme investigations, insulin and radioimmune determinations.

The glucose tolerance test should be repeated because glycoregulation abnormalities can be considered among diabetic risk factors only when they persist. In order to detect diabetes mellitus among larger communities the test should be resumed every 2 years whenever necessary [1]. The above-mentioned observations

should be taken into consideration when reading the curves. According to Justin-Besançon [18], all the curves with glucose levels exceeding 1.20 g %<sub>00</sub> at 2 hours should be considered normal if the other GTT values are within normal limits. He considers diabetic curves only those with an arrow pointing higher than 2 g %<sub>00</sub>; the curves with the arrow pointing 1.60 to 2 g %<sub>00</sub> being "paradiabetic".

There are also physiological GTT changes like those occurring during pregnancy (which disappear after birth); GTT is also impaired in other numerous conditions besides diabetes mellitus (digestive, hepatic, cardiovascular diseases, various afflictions with important metabolic dysfunctions). In the same subject, GTT curves can be sometimes "normal", at other times "abnormal" (or suspect) as authorised researches have pointed out [22]. The fluctuations which affect glucose homeostasis by means of an elevated catecholamine secretion during the test may account for the above-mentioned results [10]. The explanations are certainly more numerous [21]. Enzyme, insulin, radioimmune dosings will probably allow a better understanding of this process. Clinically, Fajans and Conn's criteria [9] are applicable to evaluating GTT curves. Nevertheless, the use of different criteria and dosing methods (Fajans and Conn dosing was based on Somogy-Nelson's method) lead to a different evaluation of the incidence of diabetes mellitus among a given population, even among researchers [10]; this requires further discussion in order to establish a uniform evaluation criterion, at least on the national level.

Considering the preservation within normal limits of the functions of glands with hyperglycemic role up to advanced ages, a larger difference between the normally preserved system and the deficient hypoglycemic one would also account for the diminished GTT in the aged. There are numerous possible interpretations of the diminished glucose tolerance among which, peripheral glucose uptake seems particularly important.

In conclusion, mention should be made of the following facts: our researches point out that increased sugar levels in clinically healthy aged subjects are not indicative of diabetes mellitus, their variation remaining within the limits admitted for mature adults; it can be interpreted in terms of an adaptative phenomenon in the course of senescence.

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**Résumé.** Les auteurs mentionnent les recherches propres et celles signalées dans la littérature médicale, concernant le processus de vieillissement en relation avec le test de tolérance vis-à-vis de la glucose; les auteurs font une interprétation de ce test. Les auteurs plaident pour une méthodologie susceptible d'uniformiser le dosage et l'interprétation des résultats, dans le domaine clinique et dans celui de la recherche fondamentale. Les perspectives des dosages enzymatiques et radio-immunologiques, dans l'explication des particularités métaboliques aux âges avancés, sont aussi considérées.

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