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7.4 Comparison between Finnish and Danish Reference Values for Plasma Proteins

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It is well known that genetic mutations may result in varying concentrations of plasma/serum proteins. Further, hormone concentrations and environmental conditions may influence on the plasma protein concentrations. Differences in plasma protein concentrations due to ethnic groups, and geography etc. in the Nordic countries may be investigated by comparing Finnish and Danish reference populations with each other. Both are of Caucasian origin but, from different groups of language and whereas the Finnish climate is belonging to the *inland* type the Danish climate is typical *coastal*. The populations in the other Nordic countries, Iceland, Norway, and Sweden, are mainly of the same ethnic group as the Danish, but the climate resembles that of Finland. The most pronounced differences might, therefore, be disclosed by comparing a Danish population with a Finnish one.

Selection of Reference Individuals

Ideal, would have been to make a study with the same design in Finland, and compare it with the Danish study (cf. sections 7.1, 7.2, and 7.3). It would, however, have been very expensive and could be viewed as too much work, considering the uncertainty of the outcome. It was decided to carry out the investigation with a smaller - but well defined group of the Finnish population - comparable to a subsample of the Danish reference group. By investigation of these selected groups major differences were thought to be easily disclosed - and even minor variations might be detected.

From the Turku region in Finland serum samples from 29 men and 27 women (not using estrogens) all of the age between 30 and 40 years, and from the Danish materials 24 samples from men and 22 samples from women (not using estrogens) in the same age group were available with sufficient serum for the comparison.

Rule in and *rule out* criteria for the reference individuals were the same as for the Danish investigation and the sampling conditions as well as the preparation of serum samples were identical (cf. section 7.2).

Analytical Design

In order to minimize analytical influence on the results of the investigation the samples were measured by the same analytical methods by the same technician in a *random set up*, where serum samples from Finnish and Danish subjects were measured *at random* in the same analytical runs in double determinations performed in separate runs.

Presentation of Data

The results are displayed on probit-plots in relation to the relevant distributions from the Danish investigation (cf. sections 7.2 and 7.3). Where no differences between the two sexes were found the results were combined, otherwise they were separated and the protein distributions are shown for both the sexes from each country.

Results

S-Prealbumin (S-Transthyretin)

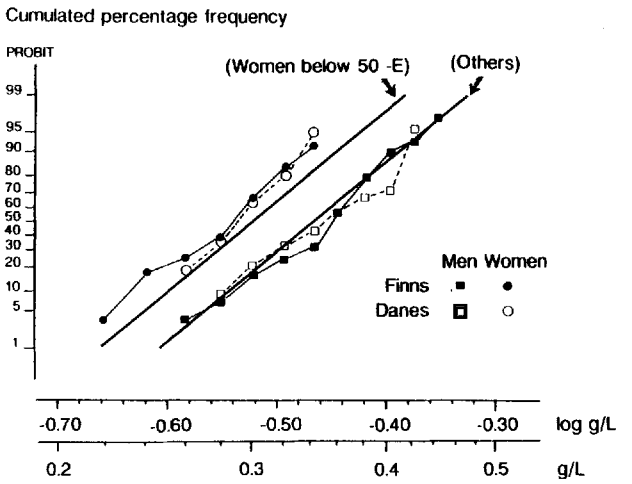

Fig. 7.4.1. *Distributions of S-Prealbumin values for the Finnish and Danish reference individuals with separate curves for the two sexes. The two straight lines indicate the distributions as estimated in the total Danish material.*

Concerning S-Prealbumin the Finnish and the Danish distributions showed differences in concentrations for men and women (below 50 years of age and not using estrogen), and the separate distributions are illustrated in Fig. 7.4.1.

The Finnish and the Danish distributions are indistinguishable and close to the distributions from the total Danish material. Therefore, it was concluded that no possible difference was detectable, and the Finnish reference interval should be identical to the Danish reference interval for S-Prealbumin.

S-Albumin

According to the Danish investigation no difference due to sex in the relevant age groups were disclosed and the sex-groups are therefore combined in Fig 7.4.2.

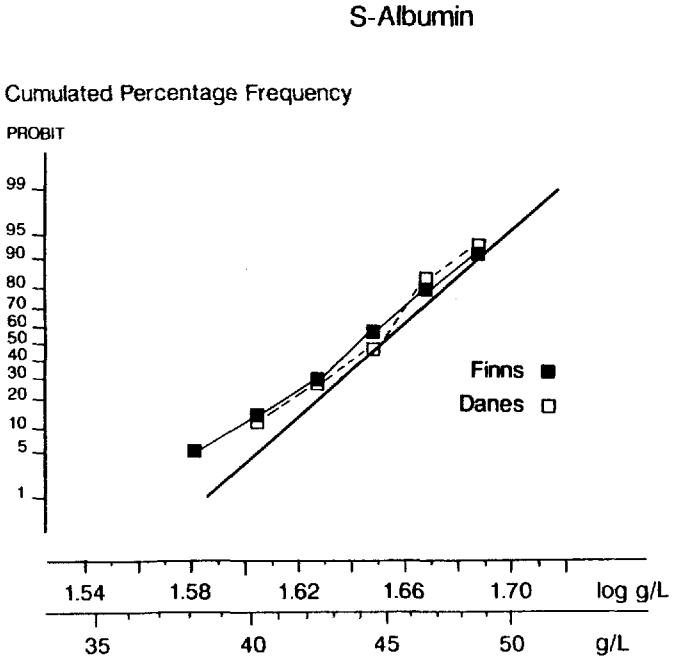

Fig. 7.4.2. *Distributions of S-Albumin values for the Finnish and Danish reference individuals. The straight line indicates the distribution as estimated in the total Danish material.*

The distributions for the Finnish and the Danish groups are indistinguishable but, both with an tendency to slightly lower values. There is, however, no reason for defining another reference interval.

S-Orosomucoid (S-α_1-Acid Glycoprotein)

Concerning S-Orosomucoid the Finnish and the Danish investigation showed differences in concentrations for men and women, and the separate distributions are illustrated in Fig. 7.4.3.

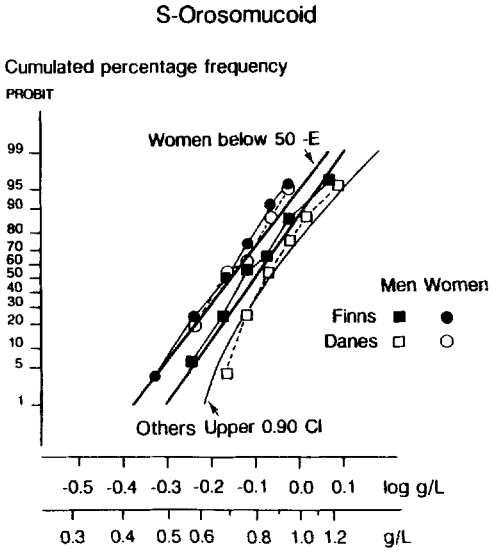

Fig. 7.4.3. *Distributions of S-Orosomucoid values for the Finnish and Danish reference individuals with separate curves for the two sexes. The two straight lines indicate the distributions as estimated in the total Danish material.*

The distributions of S-Orosomucoid for Finnish and Danish women are indistinguishable whereas, the curves for men are different. However, it is the Danish subgroup that differs from the Danish main group (indicated by the upper 0.90 confidence interval for 23 degrees of freedom), whereas, the Finnish values are distributed according to the Danish main group. In consequence, there is no reason for choosing a separate reference interval.

S-α_1-Antitrypsin (S-α_1-Proteinase Inhibitor)

According to the Danish investigation no differences due to sex for the relevant age groups were disclosed and the sex-groups are therefore combined in Fig 7.4.4.

The distributions for the Finnish and the Danish groups are indistinguishable but, both with a tendency to slightly lower values. There is, however, no reason for defining another reference interval.

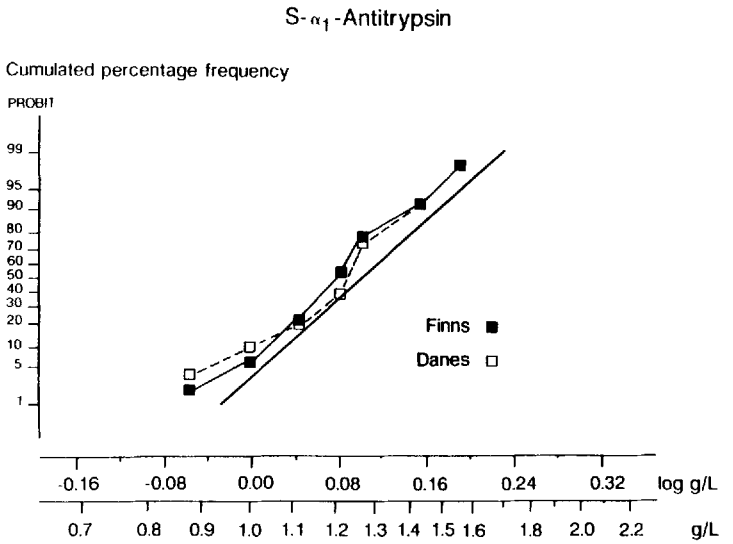

Fig. 7.4.4. *Distributions of S-α_1-Antitrypsin values for the Finnish and Danish reference individuals. The straight line indicates the distribution as estimated in the total Danish material.*

S-Haptoglobin

S-Haptoglobin is different from the previously described proteins as the distribution are not log-Gaussian, so the comparison is more difficult than for the other proteins.

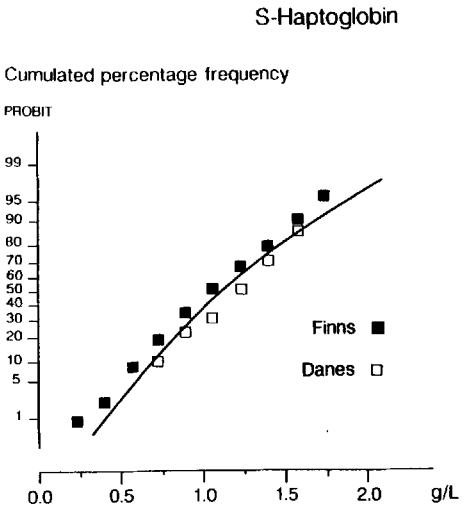

Fig. 7.4.5. *Distributions of S-Haptoglobin values for the Finnish and Danish reference individuals. The curve indicates the distribution as estimated in the total Danish material.*

The distributions of the Finnish and Danish reference groups are illustrated in Fig. 7.4.5 and compared with the curve for the total Danish distribution of S-Haptoglobin values.

The Finnish distribution is located with lower values than both the comparable subgroup and the total Danish distribution, but as this distribution is not parametric there is no simple way to illustrate the confidence intervals for the percentiles, which should be chosen non-parametric.

The difference is about 0.15 g/L along the whole distribution, and we have decided to define the reference intervals for the Finnish population accordingly with limits 0.15 g/L below the Danish values.

S-Transferrin

According to the Danish investigation no differences due to sex for the relevant age groups were disclosed and the sex-groups are therefore combined in Fig 7.4.6.

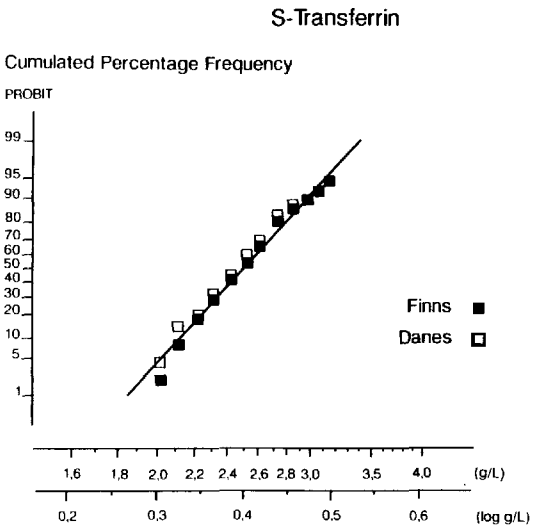

Fig. 7.4.6. *Distributions of S-Transferrin values for the Finnish and Danish reference individuals. The straight line indicates the distribution as estimated in the total Danish material.*

The distributions for the Finnish and the Danish groups are indistinguishable with a slight tendency to splitting up for the lower values, but without any convincing difference. So, there is no reason for defining another reference interval.

S-IgA

As for S-Haptoglobin, the S-IgA distributions are not directly parametric but, might be transformed to distributions close to log-Gaussian (cf. chapter 7.2).

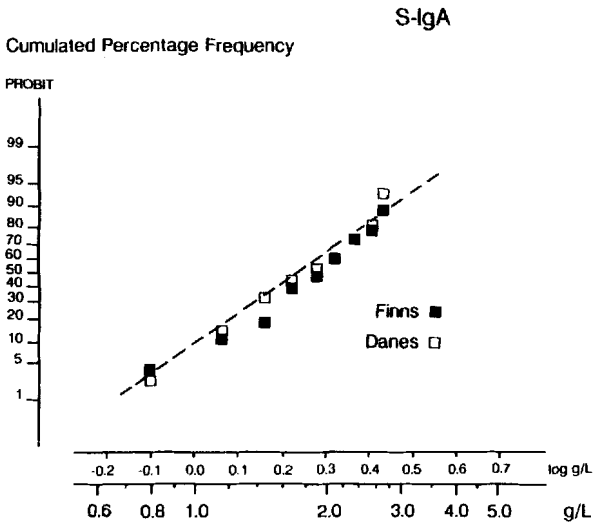

Fig. 7.4.7. *Distributions of S-IgA values for the Finnish and Danish reference individuals. The curve indicates the distribution as estimated in the total Danish material (without transformation).*

The two distributions are clearly overlapping with a slight tendency to higher values for the Finns in the middle of the distribution. There is, however, no reason for defining another reference interval for the Finns.

S-IgG

For S-IgG the Danish investigation showed differences in concentrations for women below 50 years of age and the remaining group, and the separate distributions are illustrated in Fig. 7.4.8.

The Finnish and the Danish distributions for women are indistinguishable and close to the distributions from the total Danish material for women, whereas, the Finnish men show higher values than the Danish men, who in turn are lower than the total material. Thus, there are no uniform differences between Finns and Danes and it was concluded that the Finnish reference intervals should be identical to the Danish.

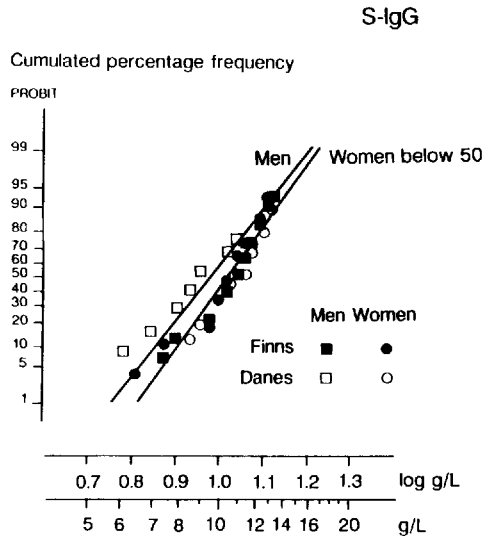

Fig. 7.4.8. *Distributions of S-IgG values for the Finnish and Danish reference individuals with separate curves for the two sexes. The two straight lines indicate the distributions as estimated in the Danish material.*

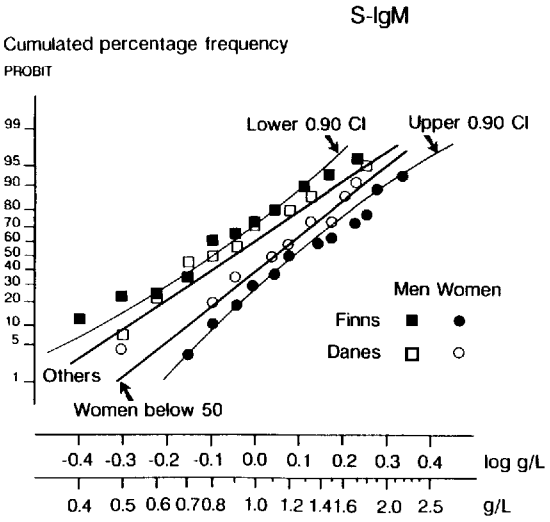

Fig. 7.4.9. *Distributions of S-IgM values for the Finnish and Danish reference individuals with separate curves for the two sexes. The two straight lines indicate the distributions as estimated in the total Danish material.*

S-IgM

For S-IgM the Danish investigation showed differences in concentrations for men and women, and the separate distributions are illustrated in Fig. 7.4.9.

The Finnish distribution for men shows lower values and the women higher values than the Danish distributions. Further, the Finnish distributions are close to the confidence intervals (shown as the lower for men and the upper for women). The results for the Finns thus seem to be contradictory. With the limited number of degrees of freedom, however, it is not possible to postulate a more pronounced difference in S-IgM values between the Finnish men and women, so the Danish reference intervals are accepted also for the Finnish population.

Discussion

The design of this comparison of plasma protein distributions between the Finnish and the Danish populations, was set up at a limited scale which could only disclose considerable differences with certainty. The results, however, gave no reasons for questioning the agreement for the plasma proteins Prealbumin, Albumin, Orosomucoid, α_1-Antitrypsin, and Transferrin.

For S-Haptoglobin the difference was clear from the present population samples - but an investigation on a larger scale might be relevant in order to confirm the difference. Unfortunately we did not investigate the frequencies of the different phenotypes in the materials as the lower values for the Finns might be related to a higher frequency of phenotype 1-1 than in the Danish population, and it might explain the difference.

Regarding the immunoglobulins, it is well known that the concentrations of these proteins in plasma are related to the environmental conditions. The results for S-IgG and S-IgM were confusing in the sense that the differences were reverse for the two sexes, making any conclusions based on the present material difficult.

In general, we have shown that in different populations it is possible to use the same reference intervals for the plasma proteins. S-Haptoglobin was an exception. It is obvious that the use of these common reference intervals are preferable to any solution based on laboratory-individual reference intervals in current use (cf. chapter 7.5).

Acknowledgements

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