NORIP
Suggested reference intervals for TOTAL PROTEIN and ALBUMIN in serum

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The working group has used the material from the NORIP data base, literature and data from the patient data base of the laboratory in evaluation of the suggested reference intervals.

Reference intervals for Total protein

Preliminary reference values suggested by NORIP (1):

Male and Female : 62 – 78 g/L

Based on partitioning criteria given by Lathi et al (2), partitioning for gender or age was not suggested.

Tietz (4): Male and female 64 – 83 g/L (ambulatory), 60 – 78 g/L (recumbent),
Age > 60 y: lowered by 2g/L. Partitioning for children < 3y

Cal target is set by reference method, DGKC (1997) (1)

Intra-individual variation: 2,7% (3)
Inter-individual variation: 4,8% (3)

Distribution of results

	Percentiles		
	2.5	**50**	**97.5**
All	62	70	78
Men, age 30-39 y	64	72	82
Men Denmark	62	70	82
All, Fürst data base – ambulatory	63	72	81

Comments to the distributions
The methods used for total protein were with few exceptions Biuret applied to different instruments. No obvious method differences between dry and wet methods were detected. Some of the laboratories using Kone instruments showed a high CV, but no results were excluded because of method differences or precision problems. 53% of the laboratories report Cal mean values outside ”minimum” bias goal.
The distribution was slighthly skewed towards higher values. A difference was found for men age 30-39, with slightly higher reference values. We could not find any explanation for this.
Country comparasion shows broader reference intervals for Danish men, especially the high value, but excluding Denmark gave no significant effect on the upper limit: 77,8 versus 77,7.

Comparison with Fürsts material of ambulatory patients shows good agreement with the NORIP data.
BMI has no effect on total protein concentration, neither has fasting.

Suggested reference intervals for Total Protein

Male and Female: 62 –78 g/L as suggested by NORIP.

Comments to the suggested reference intervals
The reference intervals are related to ambulatory persons (not recumbent).
Oral contraceptives give elevated total protein by average 0,5 g/L.
Values measured in plasma gives in average 2 g/L higher results than if measured in serum.
Children are not included in the reference material. See literature for partitioning.

Reference intervals for Albumin

Preliminary reference values suggested by NORIP (1):

Male and female: 37 – 48,3 g/L (Age < 40 y)
37 – 45,6 g/L (Age: 40 – 70 y)
35 – 45,6 g/L (Age > 70y)

Partitioning criteria given by Lathi et al. suggests no partitioning for gender, but partitioning for age for the high limit at the age of 40 and at the low limit at the age of 70.

Tietz (4): Adults: 34-48 g/L, >60 y: 32-46 g/L. Partitioning for children <14 y. Values average 3 g/L higher in ambulatory individuals.

Cal target: IMEP17-transferred value, standard uncertainty 3,26%.

Intra-individual variation: 3,1% (3)
Inter-individual variation: 5,2 % (3)

Distribution of results

	Percentiles		
	2.5	**50**	**97.5**
All	36	42	47
All < 40 y	32	43	48
All >= 40 y	36	41	46
All >= 70 y	35	40	44
All < 40 y, Fürst (ambulatory)	34	42	47
All > 40 y, Fürst (ambulatory)	33	40	45
All, non BCP – methods	37	41	47
All, BCP	35	40	46
All, non BCP - methods (Oral contrac.)	36	41	46
All, BCP (Oral contrac.)	35	39	44

Comments to the distributions
The albumin reference values show a market- and continous reduction with age.
Albumin is analyzed basicaly with four different methods on a variety of instruments, BCG (bromcresolgreen), BCP (bromcresolpurple), immunological method and dry chemistry (BCG) on Vitros. 73% of the laboratories report Cal mean value outside ”minimum” bias goal.
All the methods performed satisfactory and no instruments, methods or country results were excluded. Having focus on the lower reference limit as the medically important one, it seemed that there is a slight method difference between BCP and the other methods of 1 – 1,5g/L.
For the BCP, oral contraceptives seems to interfere with the method.
In addition the physiological value of albumin decreases by approximately 1g/L in individuals on oral contraceptive treatment.
Comparison with Fürst material (BCG) on ambulatory patients show good agreement with the NORIP data.
BMI and fasting have no market effect on albumin values.

Suggested reference intervals for Albumin

Male and Female: 37 – 48 g/L (Age < 40 y)
37 – 46 g/L (Age > 40-70 y)
35 – 46 g/L (Age > 70 y)

Alternative: From a medical point of view it would be acceptable and practical if the high reference limit is set to a common value of f.ex. 48g/L.

Comments to the suggested reference intervals
The reference intervals are related to ambulatory persons (not recumbent).
Oral contraceptives lower the values by app.1 g/L.
No significant difference in albumin measured in plasma and serum.
The BCP-method may need special attention.
Children are not included in the reference material. See literature for partitioning.

References:

1. Rustad, P.: Nordic reference interval project. http://www.furst.no/norip
2. Lathi A, Hyltoft Pettersen P, Boyd JC, Fraser CG, Jørgensen N: Objective criteria for partitioning Gaussian-distributed reference values into subgroups, Clin Chem 2002; 48: 338-52.
3. Ricos C,et al.: Current databases on biological variation: pros, cons and progress. SJCLI 1999; 59.
4. Tietz Textbook of Clinical Chemistry, 3.ed, W.B.Saunders Co.,1999.
5. Fürst Med Lab: Patent result database, Nov.2002 and Feb.2003.