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A Fully Automated Serum Electrophoresis System

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Summary: This report summarizes an evaluation of the fully automated Olympus Hite System (AHS, Olympus, D-2000 Hamburg) for serum protein fractionation. The precision thereof exceeded that of the semi-manually processed Multiphorese System II MS 755 (Vogel, D-6300 Gießen). It proved to be rapid and easy to maintain. A comparison of the albumin values obtained by AHS and Beckman immunochemistry system showed a good correlation between both methods.

Ein vollautomatisches Serum-Elektrophorese System

Zusammenfassung: Es wird über die Erprobung des vollautomatischen Olympus Hite Systems (AHS, Olympus, D-2000 Hamburg) für die Serum-Protein-Fraktionierung berichtet. Die Präzision dieses Gerätes war besser als die eines zum Vergleich verwendeten halb-mechanisierten Systems (Multiphorese System II MS 755 (Vogel, D-6300 Gießen). Es erwies sich als rasch und einfach in der Bedienung. Ein Vergleich der Albuminwerte, welche mit dem AHS und dem Beckman Immunochemistry System erhalten wurden, ergab eine gute Übereinstimmung beider Verfahren.

Introduction

Electrophoresis by separation of serum proteins on cellulose-acetate membrane is widely used for the clinical screening and monitoring of abnormal protein patterns (1). The intricate semi-manually processed techniques (2, 3), however, show poor duplication with aliquots of the same specimens. In addition, interlaboratory variation, partly dependent on methodology, showed deviant results, thus preventing comparison of electrophoretic data from different laboratory centres. The clinical diagnostic value of the former systems was also diminished by the non-linearity between the relative albumin and globulin concentrations and total serum protein concentrations (4). Furthermore, the handling of the potential cancerogen dioxan for membrane transparency prior to densitometry should be avoided (5).

The present study was undertaken to evaluate, according to the recommendations of IFCC (6), the fully automated Hite-system (AHS, Olympus, D-2000 Hamburg), to assess a series of reference values for healthy adults, and to compare the albumin values obtained by the candidate method with those found with the Beckman Immunochemistry system.

Materials and Methods

Origin of specimens

Sera were randomly drawn from 200 hospitalized subjects and tested in parallel using the AHS and the currently employed semi-manually processed technique as described below. For setting up the reference range, sera were obtained from 335 apparently healthy adults comprising 176 blood donors (age range: 22–42 years, sex ratio: male/female, 3/2) and 159 healthy staff members (age range: 20–60 years) routinely examined by personnel medical service. Laboratory information about these individuals based on haemogram (erythrocyte and leucocyte count, haemoglobin, haematocrit), aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase, hepatitis B surface (HB_s) antigen and anti-HB_s-antibody yielded normal values in all cases. All sera were tested within 48 h of collection.

Electropherograms

The reagents of the AHS acetic acid (997 g/l) (No. 33209), decahydronaphthalene (No. 803101) and granular activated charcoal (No. 2515) were supplied by E. Merck (D-6100 Darmstadt), cellulose-acetate membranes (SM 11200) and 0.07 mol/l sodium-barbital buffer pH 8.6 containing citric acid 50 g/l (No. 14202) (diluted with 900 ml of bidistilled water for the electrophoresis chamber; diluted with 1000 ml of bidistilled water for the premoistening roller chamber) by Sartorius (D-3400 Göttingen), heat sensitive recording paper (No. 60082) and Ponceau S 8 g/l in trichloroacetic acid 60 g/l (No. 60098) by Olympus (D-2000 Hamburg). To obtain electro-

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phoretic patterns, 50 µl of sera were pipetted onto capillary blades of a sample plate, which was then set into the apparatus. All successive, previously manually-processed steps, such as serum application, switch on/off the power supply for the electrophoresis chamber, staining, destaining, membrane transparency, drying, densitometry and recording were performed automatically.

For comparison, the electrophoretic patterns were displayed by the semi-manually processed Multiphorese-System II MS 755 (SMMS, Vogel, D-6300 Gießen). The reagent, 0.07 mol/l sodium-barbital buffer pH 8.6 containing citric acid (50 g/l) (diluted with 1000 ml of bidistilled water) (No. SM 14202) and cellulose-acetate membranes (No. SM 11200) were purchased from Sartorius (D-3400 Göttingen). The electrophoresis chamber (No. 49002-01), multi-sample applicator for simultaneous application of 8 samples (No. 49010-80) and the staining solution, Amido Black 10 B (No. 49718-06), were supplied by Instrumentation Laboratory GmbH (D-5303 Bornheim-Hersel). The destaining reagents, acetic acid (997 g/l) (No. 33209) and methanol (No. 6009) mixed 1 + 9 by vol., as well as the solution for transparency, dioxan/isobutanol (No. 3111), were supplied by E. Merck (D-6100 Darmstadt).

Protein measurements

Albumin was quantitated by rate nephelometry (Beckman Immunochemistry system (ICS), analyzer 662401) of the immuno-precipitin reactions after adding monospecific anti-human albumin serum (Beckman, D-8000 München) to sera. Total serum protein was determined by the biuret reaction (7).

Control materials

REL (catalogue No. CLK 6213) were purchased from Asid-Bonz & Sohn (D-8044 Unterschleißheim), Precilip (catalogue No. 125059) from Boehringer Mannheim (D-6800 Mannheim), Kontrollogen L (catalogue No. ORTL 02057) from Behring-Werke (D-3550 Marburg), Hyland N (catalogue No. HD-0450135) and Hyland P (catalogue No. HD-045-119) from Hyland-Travenol GmbH (D-8000 München).

Statistical methods

Precision within-run and between-days (mean value: $\bar{x}$, standard deviation: S.D., coefficient of variation: C.V.) as well as the χ^2 test for goodness of fit for the normal distribution, linear regression analysis, standardized principle component analysis (8) and *Student*'s t-test (statistical difference from zero: $2\,p < 0.05$) were performed as described elsewhere (9).

Results and Discussion

Imprecision

The control materials fractionated by the AHS revealed a lower within-run imprecision for albumin (C.V.: 0.75% to 0.98%) and γ-globulin (C.V.: 0.32% to 2.2%) with respect to the SMMS (albumin, C.V.: 1,82% to 3.56%; γ-globulin, C.V.: 4.97% to 20.36%) (tab. 1, 2). Furthermore, the latter system showed incomplete separation in 4 out of 5 control materials. The between-days imprecision (C.V.) for the AHS varied from 0.76% to 1.78% for the albumin fraction and from 1.85% to 5.48% for the γ-globulin fraction (tab. 1).

Inaccuracy

The means in table 1 for the albumin, α_1-, α_2-, and γ-globulin fractions correlated sufficiently with the assigned values. Constantly decreased values (between 18.5% to 34%) with regard to the assigned values were found for the β-globulin fraction. The relation between total serum protein and densitometric results (linearity test) was analyzed by diluting serially control materials and sera with various total serum protein concentrations. While no relevant relative deviation of densitometric results (< 2%) was observed for all fractionated samples with the AHS, a reduced range of linearity was found with the SMMS, yielding an increase of the fraction of albumin in relation to the degree of dilution (fig. 1).

The inaccuracy was further investigated by comparison of the fractions of albumin and γ-globulin from various healthy adults, using the AHS and the SMMS (fig. 2a, b). The results indicate that the fractions of albumin and γ-globulin differed significantly between AHS and SMMS. The albumin concentrations in various samples of healthy adults were measured with the AHS, the SMMS and the Beckman ICS respectively. The absolute albumin concentrations in samples tested by both electrophoretic systems were calculated via the relative albumin values from total serum protein (fig. 3a, b).

In contrast to the albumin values obtained with the SMMS, those found with the AHS showed no significant difference from that of the Beckman ICS. Based upon these observations, it was compulsory to establish a new reference range for AHS.

Carry over effects

The percental coefficient of carry over determined according to *Hjelm* (10) was 0.84% for low to high albumin values and 0.05% for high to low albumin values. The ninhydrin colour reaction for the detection of carried over proteins was negative (11). Therefore, carry over for the AHS was concluded to be negligible.

Interference from endogeneous compounds

No interference was noticed from haemoglobin (up to 2.3 g/l), cholesterol (up to 11.9 mmol/l), triglycerides (up to 12.37 mmol/l) and bilirubin (up to 259 µmol/l) in sera assayed by the AHS. However, the electrophoretic separation with the SMMS was incomplete for haemolytic (haemoglobin above 0.5 g/l) and lipaemic sera (cholesterol above 6.2 mmol/l, triglycerides above 2.84 mmol/l). No interference was observed for bilirubinaemic sera using AHS and SMMS.

Interference from exogeneous compounds

Pooled sera from several patients were spiked with 48 different drugs or anticoagulants in clinically relevant concentrations (12) (tab. 3). The confidential range was determined from 20 electrophoretic determinations in

Tab. 1. Precision data of the electrophoretically fractionated control materials determined with the AHS.

	Protein fractions				
	Albumin	α_1-Globulin	α_2-Globulin	β-Globulin	γ-Globulin
Control serum: REL (lot. No. 405A)					
Assigned value (range)	0.702 (0.597–0.807)	0.021 (0.0158–0.0262)	0.0536 (0.0429–0.0643)	0.0710 (0.0568–0.0852)	0.152 (0.122–0.182)
Imprecision within run[1])					
$\bar{x}$	0.715	0.020	0.062	0.0581	0.1462
C.V.	0.52	5.0	1.02	1.7	1.7
n	20	20	20	20	20
Imprecision between days[2])					
$\bar{x}$	0.7092	0.0211	0.0568	0.0579	0.1509
C.V.	1.17	5.2	2.8	4.8	2.66
n	10	10	10	10	10
Control serum: Precilip (lot. No. 661)					
Assigned value (range)	0.642 (0.578–0.706)	0.036 (0.029–0.043)	0.103 (0.082–0.124)	0.103 (0.082–0.124)	0.116 (0.092–0.139)
Imprecision within run[1])					
$\bar{x}$	0.6558	0.0407	0.0962	0.0683	0.1388
C.V.	0.27	2.2	1.03	1.61	1.22
n	19	19	19	19	19
Imprecision between days[2])					
$\bar{x}$	0.6594	0.0396	0.0954	0.0754	0.1379
C.V.	0.76	3.78	2.93	5.9	5.48
n	10	10	10	10	10
Control serum: Kontrollogen L (lot. No. 3105)					
Assigned value (range)	0.620 (0.57–0.67)	0.030 (0.015–0.045)	0.080 (0.06–0.10)	0.115 (0.065–0.165)	0.155 (0.125–0.185)
Imprecision within run[1])					
$\bar{x}$	0.659	0.0357	0.0867	0.0757	0.1422
C.V.	0.97	3.9	1.62	1.71	0.33
n	18	18	18	18	18
Imprecision between days[2])					
$\bar{x}$	0.6515	0.0358	0.086	0.0759	0.1503
C.V.	1.04	4.2	2.67	6.2	2.86
n	10	10	10	10	10
Control serum: Hyland N 11					
Assigned value (range)	0.625 (0.578–0.672)	0.034 (0.026–0.042)	0.089 (0.067–0.111)	0.098 (0.075–0.121)	0.156 (0.133–0.179)
Imprecision within run[1])					
$\bar{x}$	0.6519	0.0326	0.0833	0.0679	0.1565
C.V.	0.98	3.2	2.4	2.09	0.32
n	19	19	19	19	19
Imprecision between days[2])					
$\bar{x}$	0.6512	0.037	0.0823	0.0708	0.1487
C.V.	1.78	3.2	5.5	2.76	4.17
n	10	10	10	10	10
Control serum: Hyland P 11					
Assigned value (range)	0.634 (0.574–0.694)	0.031 (0.021–0.041)	0.090 (0.063–0.117)	0.093 (0.070–0.116)	0.147 (0.135–0.159)
Imprecision within run[1])					
$\bar{x}$	0.6646	0.0265	0.0764	0.0719	0.1446
C.V.	0.81	4.5	2.2	2.48	1.85
n	19	19	19	19	19
Imprecision between days[2])					
$\bar{x}$	0.6682	0.0316	0.0825	0.0704	0.1515
C.V.	1.27	8.5	2.78	2.8	2.2
n	10	10	10	10	10

[1]) $\bar{x}$ = Protein fraction, mean value
C.V. = Coefficient of variation (in %)
n = Number of determinations

[2]) $\bar{x}$ = Protein fraction, mean value
C.V. = Coefficient of variation (in %)
n = Number of days

Tab. 2. Precision data of the electrophoretically fractionated control materials determined with the SMMS.

	Protein fractions				
	Albumin	α_1-Globulin	α_2-Globulin	β-Globulin	γ-Globulin
Control serum: REL (lot. No. 405A)					
Assigned value (range)	0.664 (0.564–0.764)	0.0270 (0.0208–0.0332)	0.0558 (0.0446–0.0670)	0.0769 (0.0615–0.0923)	0.176 (0.141–0.211)
Imprecision within run[1])					
$\bar{x}$	0.6975	i.s.*	i.s.	0.0628	0.145
C.V.	1.84			3.50	5.2
n	10	10	10	10	10
Control serum: Precilip (lot. No. 662)					
Assigned value (range)	0.623 (0.561–0.685)	0.033 (0.0264–0.0396)	0.093 (0.0744–0.112)	0.095 (0.0760–0.114)	0.156 0.125–0.187)
Imprecision within run[1])					
$\bar{x}$	0.610	0.0406	0.1043	0.0995	0.11
C.V.	3.0	9.36	15.05	22.09	20.36
n	10	10	10	10	10
Control serum: Kontrollogen L (lot. No. 3105)					
Assigned value (range)	0.590 (0.54–0.64)	0.03 (0.02–0.04)	0.095 (0.08–0.11)	0.11 (0.095–0.125)	0.18 (0.15–0.21)
Imprecision within run[1])					
$\bar{x}$	0.610	i.s.	i.s.	i.s.	0.16
C.V.	5.83				18.12
n	10	10	10	10	10
Control serum: Hyland N 11					
Assigned value (range)	0.629 (0.582–0.676)	0.033 (0.023–0.043)	0.087 (0.07–0.104)	0.099 (0.073–0.125)	0.155 (0.115–0.195)
Imprecision within run[1])					
$\bar{x}$	0.6475	i.s.	i.s.	i.s.	0.1263
C.V.	3.05				15.20
n	10	10	10	10	10
Control serum: Hyland P 11					
Assigned value (range)	0.637 (0.567–0.707)	0.028 (0.023–0.033)	0.079 (0.062–0.096)	0.095 (0.076–0.114)	0.159 (0.128–0.190)
Imprecision within run[1])					
$\bar{x}$	65.38	i.s.	i.s.	0.0749	0.1238
C.V.	3.26			6.0	4.97
n	10	10	10	10	10

[1]) $\bar{x}$ = Protein fraction, mean value
C.V. = Coefficient of variation (in %)
n = number of determinations
*i.s. = incomplete separation

the absence of any compounds. No interference was found with the tested antirheumatic, cytostatic, cardioactive, antihypotonic and diuretic drugs. The recovery of albumin in the presence of acidum ascorbicum and chlordiazepoxidum was low. For the α_1- and α_2-globulin fractions, minor deviations outside the confidential range were found in the presence of salicylazosulphapyridinum, indometacinum, acidum ascorbicum, dextranum 6%, chloramphenicolum, benzbromaronum, acidum triiodozoicum, allopurinolum, Na-fluoratum, Na-oxalicum, and chlordiazepoxidum. At present any interference from drugs and their clinical relevance must be ascertained individually.

Reference range

Our results are mainly in agreement with the reported ranges for albumin, α_1-, α_2-, β- and γ-globulin fractions from blood donors (4). Investigations on medical staff yielded broader ranges, especially for the albumin and

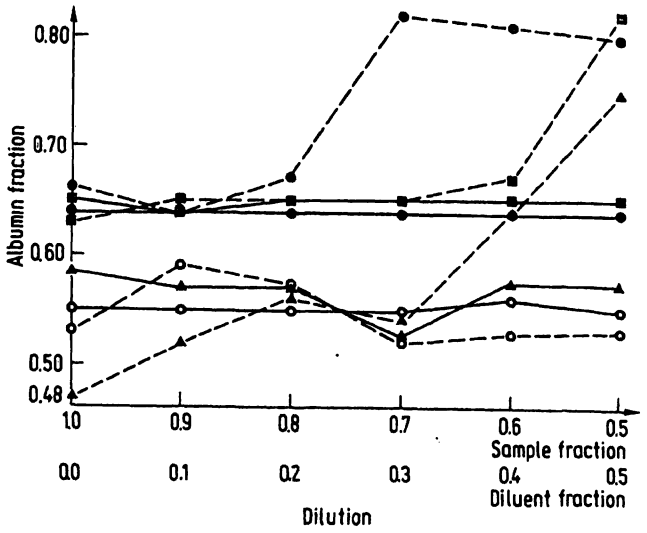

Fig. 1. Linerarity pattern of the albumin fraction with regard to the degree of dilution (diluent: 0.15 mol/l NaCl) of the applied total serum protein in control materials (e.g. Kontrollogen L, Hyland N 11, Hyland P 11, ■) and sera with various protein concentrations (total serum protein: ▲ < 55 g/l, ● 60–75 g/l, ○ > 80 g/l) performing AHS (——) and SMMS (- - -).

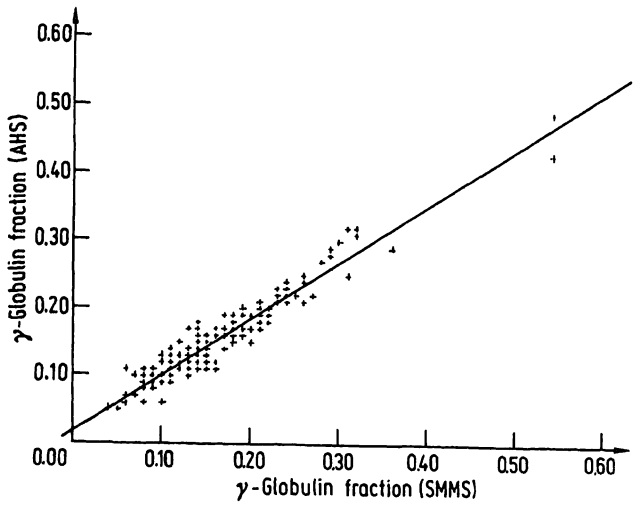

Fig. 2b. Correlation between the γ-globulin fractions obtained by SMMS and AHS. Linear regression analysis: slope = 0.89, intercept = 0.0169, r = 0.96, $\bar{x}$ = 0.1557, S.D. = 0.0723, $\bar{y}$ = 0.1483, S.D. = 0.0632, n = 200. Standardized principle component analysis: slope = 0.87, intercept = 0.0122. Paired t-test: t = −5.19, 2p < 0.001.

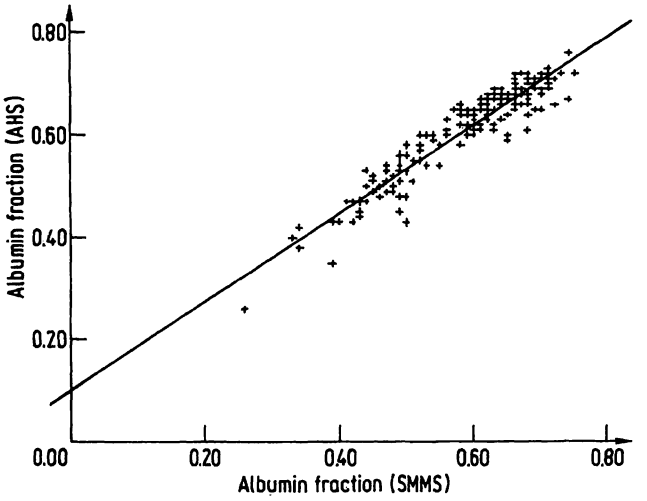

Fig. 2a. Correlation between the albumin fractions obtained by SMMS and AHS. Linear regression analysis: slope = 0.87, intercept = 0.098, r = 0.95, $\bar{x}$ = 0.5943, S.D. = 0.0962, $\bar{y}$ = 0.6167, n = 200. Standardized principle component analysis: slope = 0.92, intercept = 0.0687. Paired t-test: t = −10.05, 2p < 0.001.

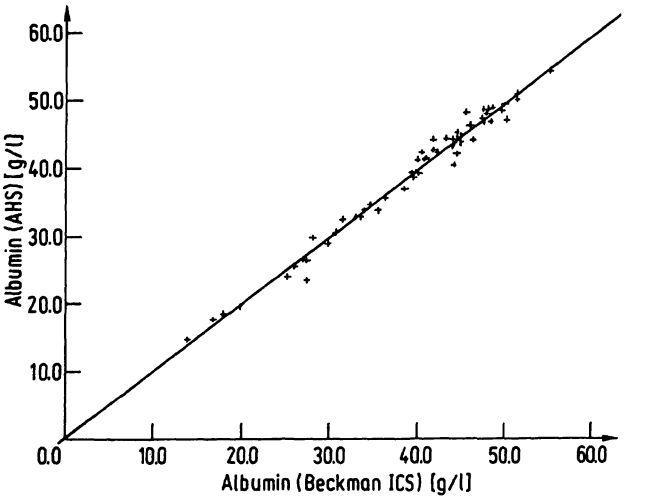

Fig. 3a. Correlation between the albumin concentrations (g/l) obtained by Beckman ICS and AHS. Linear regression analysis: slope = 0.99, intercept = 0.22, r = 0.99, $\bar{x}$ = 39.48, S.D. = 9.31, $\bar{y}$ = 39.49, S.D. = 9.34, n = 61. Standardized principle component analysis: slope = 1.00, intercept = 0.12. Paired t-test: t = −0.07, 2p > 0.05.

γ-globulin fractions. Considering the lack of definitive criteria for defining a population of apparently healthy adults, we regarded those individuals as healthy, who showed no uncommon data from anamnesis, physical examination and 9 laboratory routine tests as described in the methodology. We calculated the values of both groups, thereby gaining a representative reference range (tab. 4). We tested the null hypothesis that the albumin, α_1-, α_2-, β- and γ-globulin fractions fit a normal distribution. Since our computed χ^2 values were not significant for albumin α_2-, β- and γ-globulin fractions at the 5% significance level, we concluded that the null hypothesis for these protein fractions has to be accepted. In the case of the α_1-globulin fraction we had to reject the null hypothesis, because the α_1-globulin fraction does not follow a normal distribution (fig. 4).

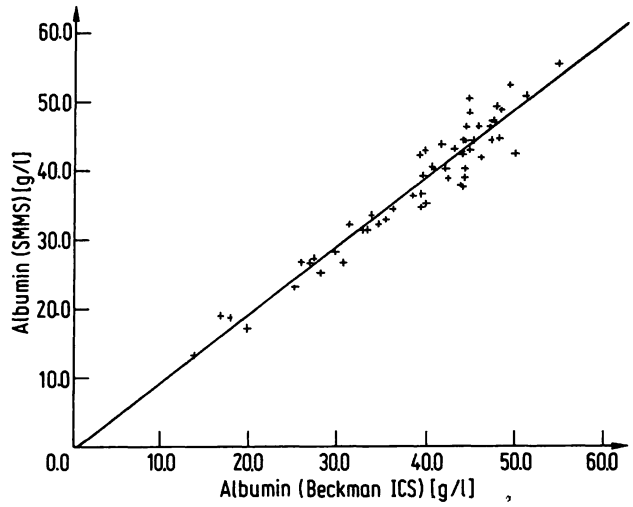

Fig. 3b. Correlation between the albumin concentrations (g/l) obtained by Beckman ICS and SMMS. Linear regression analysis: slope = 0.98, intercept = −0.46, r = 0.96, $\bar{x}$ = 39.39, S.D. = 9.24, $\bar{y}$ = 38.11, S.D. = 9.39, n = 61. Standardized principle component analysis: slope = 1.02, intercept = −1.92. Paired t-test: t = 3.98, 2p < 0.001.

Practicability

The time for setting up one sample is 75 min, for 100 samples 180 min and for 200 samples 300 min. The maximum number of samples is 100 before the AHS requires a recharge. The application dosage is 0.6 µl per sample but the capillary blades must be charged with 30–50 µl per sample. At present the AHS can only analyse sera. Work is in progress on the electrophoretic determination of proteins in other body fluids. The odour of decahydronaphthalene has been eliminated by using granular activated charcoal and an automatic vent pipe. The handling of AHS is simple. The manufacturer provides a detailed operating manual as well as a tool box with hints on minor repairs.

Not considering the initial purchase and other fixed costs, the following variable costs for a serum electrophoretic determination including reagents, control sera, pertinent supplies and technician's time are about 0.83 DM for AHS and about 1.87 DM with the SMMS in a series of 100 samples (tab. 5).

Conclusion

AHS showed a significantly better accuracy, practicability and lower imprecision with regard to manual systems such as SMMS. Albumin values obtained by AHS and Beckman ICS showed a good correlation. In addition, AHS reduced the personal work load thereby increasing the sample throughput per day and proved

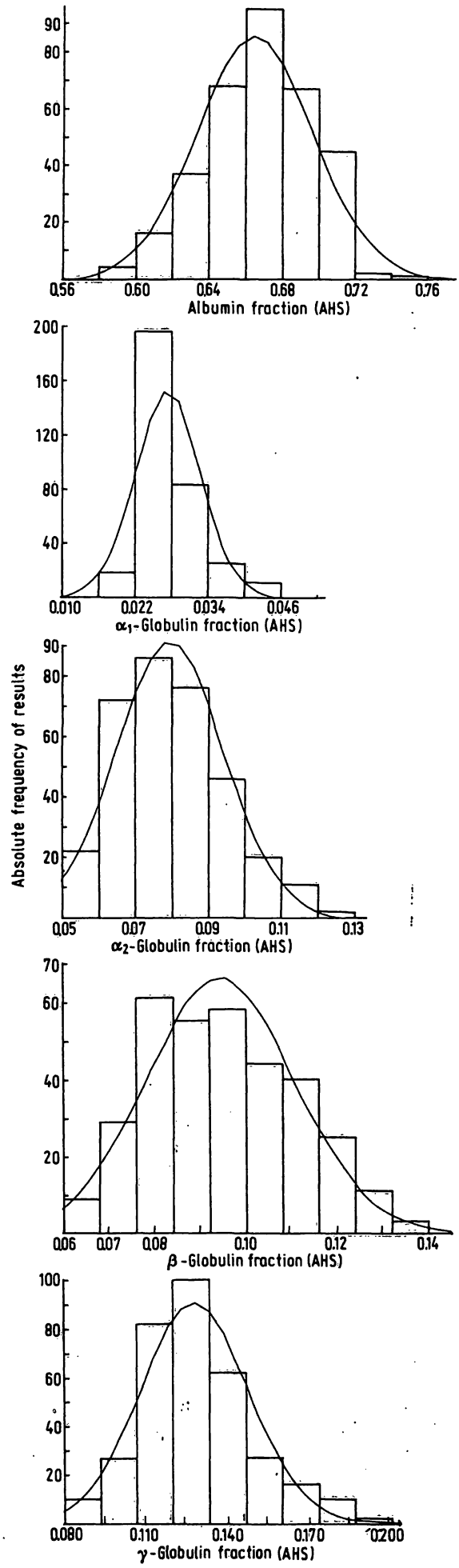

Fig. 4. Histograms representing the distribution of the albumin, α_1-, α_2-, β- and γ-globulin fractions obtained by AHS.

Tab. 3. Recovery of AHS fractionated albumin-, α_1-, α_2-, β- and γ-globulins in human pooled sera containing various drugs. As controls a mean value and the range of 3 standard deviations was calculated from 20 electrophoretic determinations of pooled sera. (Albumin: 0.597–0.628; α_1-Globulins: 0.029–0.036; α_2-Globulins: 0.106–0.115; β-Globulins: 0.0635–0.0791; γ-Globulins: 0.154–0.191. Values outside this range are considered as due to interference (marked by asterisks).

Trade Name	I.N.N.[1])	Drug concentration (g/l)	Protein fractions			
			Albumin	α_1-Globulins	α_2-	β-	γ-
Azulfidine	salicylazosulphapyridinum	1600	0.623	0.033	0.104*	0.068	0.172
Ammuno	indometacinum	40	0.620	0.029*	0.109	0.068	0.174
Aldactone	spironolactonum	80	0.615	0.033	0.115	0.070	0.167
Alkeran	mephalanum	1.5	0.624	0.023*	0.112	0.074	0.167
Aponal	doxepinum	60	0.621	0.031	0.109	0.072	0.168
Aspirin	acidum acetylosalicylicum	1000	0.616	0.031	0.110	0.071	0.172
Benemid	probenecidum	400	0.617	0.033	0.112	0.073	0.165
Biligrafin	adipinyltriiod-anilidum	2000	0.612	0.032	0.114	0.069	0.162
Binotal 500	aminobenzyl-penicillinum	1800	0.609	0.031	0.111	0.071	0.177
Buscopan	hyoscin-N-butyl-brominum	20	0.603	0.032	0.114	0.073	0.178
Butazolidine	phenylbutazonum	120	0.598	0.034	0.114	0.074	0.180
Cebion	acidum ascorbicum	800	0.585*	0.037*	0.114	0.074	0.190
Dulcolax	bisacodylum	2	0.615	0.032	0.112	0.072	0.169
Durenat	sulfanilamido-pyrimidinum	200	0.620	0.031	0.108	0.068	0.172
Endoxan	cyclophosphamidum	80	0.621	0.032	0.110	0.070	0.168
Euglucon 5	glibenclamidum	3	0.624	0.032	0.108	0.067	0.169
Furadantin	nitrofurantoinum	50	0.615	0.032	0.111	0.067	0.174
Hostacyclin	tetracyclinum	400	0.625	0.030	0.106	0.070	0.169
Intensain	carbocromenum	180	0.621	0.032	0.109	0.077	0.162
Lanicor	digoxinum	0.15	0.621	0.031	0.108	0.068	0.172
Lasix	furosemidum	400	0.620	0.031	0.108	0.069	0.172
Luminal	acidum phenylaethyl-barbituricum	60	0.622	0.032	0.110	0.069	0.167
Macrodex 6%	dextranum 6%	18000	0.609	0.030	0.105*	0.074	0.181
Marcumar	phenprocoumonum	3.6	0.614	0.031	0.109	0.071	0.175
Megaphen	phenothiazinum	200	0.618	0.031	0.110	0.072	0.169
Metalcaptase	*D*-penicillaminum	360	0.621	0.031	0.108	0.069	0.171
Methotrexat	acidum methylpteroyl-glutaminicum	80	0.619	0.032	0.108	0.069	0.172
Modenol	thiabutazide etc	1.98	0.608	0.035	0.108	0.069	0.181
Nicobion	nicotinamidum	120	0.612	0.033	0.106	0.069	0.180
Novadral	norfenefrinum	4.8	0.606	0.032	0.111	0.070	0.182
Novalgin	novaminsulfonum	800	0.607	0.030	0.107	0.069	0.188
Paraxin	chloramphenicolum	6000	0.604	0.030	0.104*	0.066	0.195
Polybion	Vitamin B complex	23.3	0.605	0.033	0.111	0.071	0.180
Prolixan 300	azopropazondihydrat	360	0.613	0.031	0.106	0.068	0.182
Resochin	chloroquinum	50	0.603	0.032	0.110	0.072	0.183
Sembrina	α-methyldopa	800	0.611	0.035	0.109	0.072	0.172
Solu-Decortin H	prednisolonum	7.2	0.621	0.030	0.076*	0.100	0.173
Tanderil	oxyphenbutazonum	120	0.605	0.033	0.110	0.071	0.181
Tolbutamid	tolbutamidum	400	0.603	0.031	0.110	0.067	0.188
Uricovac	benzbromaronum	80	0.621	0.034	0.099*	0.079	0.166
Urografin	acidum triiodbenzoicum	6080	0.614	0.037*	0.091*	0.080	0.168
Zyloric	allopurinolum	180	0.619	0.037*	0.101*	0.079	0.165
Na-Citrat	Na-citricum	5000	0.610	0.033	0.108	0.069	0.180
Na-Fluorid	Na-fluoratum	2000	0.613	0.032	0.105*	0.070	0.180
Na-Oxalat	Na-oxalicum	3000	0.615	0.034	0.105*	0.070	0.176
Liquemin	Na-heparinicum	750	0.610	0.033	0.107	0.078	0.172
EDTA	Titriplex III	1000	0.611	0.032	0.110	0.066	0.182
Multum	chlordiazepoxidum	18	0.596*	0.031	0.104*	0.073	0.196

[1]) I.N.N. = International non-proprietary names as proposed by the WHO (13).

Tab. 4. Reference values of serum protein fractions obtained by AHS.

Protein fraction	Blood donors n = 176 $\bar{x}$ ± 2 S.D. (95%) range	Staff members n = 159 $\bar{x}$ ± 2 S.D. (95%) range	Overall mean n = 335 $\bar{x}$ ± 2 S.D. (95%) range	n = 335 $\bar{x}$
Albumin	0.621 –0.724	0.5902–0.7354	0.6015–0.7236	0.6648
α_1-Globulin	0.193–0.0325	0.0153–0.0429	0.0173–0.0384	0.0274
α_2-Globulin	0.053–0.099	0.0555–0.1303	0.0513–0.1129	0.0790
β-Globulin	0.0679–0.1239	0.0591–0.1458	0.0598–0.1438	0.0940
γ-Globulin	0.0941–0.1637	0.0750–0.1980	0.0860–0.1795	0.1340

Tab. 5. Comparison of the costs of AHS and SMMS. n = number of specimens per series.

	AHS			SMMS		
n	1	10	100	1	10	100
Technician time[1]) (DM)	1.80	0.60	0.59	6.85	1.74	1.22
Reagents, control sera and pertinent supplies (DM)	6.00	0.60	0.29	2.20	0.77	0.65
Total (DM)	7.80	1.20	0.83	9.05	2.51	1.87

[1]) costs per minute technician time 0.60 DM (14).

to be reliable and easier to maintain than SMMS. The results of this study showed AHS to be very suitable for serum protein fractionation.

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