a result of 0.50 mg/L, exceeding the manufacturer's suggested threshold for this assay of 0.30 mg/L, and thus would have been reported as positive for amphetamine.

Confirmatory testing was performed by thin-layer chromatography (Toxi-Lab Drug Detection System; Analytical Systems, Division of Marion Laboratories, Inc., Laguna Hills, CA 92653), and results were compared with the following information offered by the manufacturer: Ritodrine migrates close to meperidine on Toxi-Lab A, stage I color with concentrated sulfuric acid is gray/sandy, stage II color with distilled water is light brown, drug absorbs ultraviolet light at stage III, and stage IV color with modified Dragendorff's reagent is yellow-brown (*3*). Testing of the patient's specimen produced results that matched these characteristics, whereas no other amphetamine or amphetamine-like compounds were detected.

Ritodrine hydrochloride, 10 mg/mL in sterile solution, was diluted 1:10 with isotonic saline to produce a 1 g/L standard. Subsequent dilutions were made with drug-free urine to obtain concentrations of 500, 375, 250, 100, 50, and 12.5 mg/L. Each of the dilutions was assayed in duplicate and the urine specimen used for the dilutions was also assayed. The following tabulation shows the results.

Ritodrine added	Amphetamine measured	Cross-reactivity,[a]
mg/L		%
375.0	2.43	0.6
375.0	2.49	0.7
250.0	1.58	0.6
250.0	1.60	0.6
100.0	0.54	0.5
100.0	0.59	0.6
50.0	0.30	0.6
50.0	0.30	0.6
12.5	0.15	1.2
12.5	0.17	1.4
0.0	0.02	—

[a] Calculated by dividing the measured amphetamine result by the ritodrine concentration and multiplying by 100.

An ADx amphetamine/methamphetamine assay of 0.50 mg/L corresponds to a ritodrine concentration of approximately 83 mg/L (0.50/0.006) when using the cross-reactivity of 0.6%. The manufacturer has tested an extensive list of compounds at various concentrations for cross-reactivity. Substances other than amphetamine, methamphetamine, and amphetamine metabolites that produced a value above the threshold of 0.30 mg/L include fenfluramine, isometheptene, isoxsuprine, labetalol, mephentermine, methylenedioxyethylamphetamine, nylidrin, phenethylamine, phenmetrazine, phentermine, propylhexedrine, and tyramine. Ritodrine is not listed in the ADx Operator's Manual as a cross-reacting substance (*4*).

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Interference with Measurement of Intact Parathyrin in Serum from Renal Dialysis Patients, *B. A. Dilena and G. H. White* (Dept. of Biochem. and Chem. Pathol., Flinders Med. Centre, Bedford Park, South Australia, 5042, Australia)

In patients with chronic renal failure who require maintenance hemodialysis, measurement of bioactive parathyrin (PTH) in serum would be a useful in vitro test for assisting the diagnosis of secondary or tertiary hyperparathyroidism. However, currently available commercial kits for assay of PHT measure immunoreactive PTH in various combinations of intact, amino-terminal, mid-molecule, or carboxy-terminal fragments, depending on antiserum specificity. The assays that detect middle and carboxy-terminal (C-terminal) fragments are of no diagnostic value in dialysis patients because the diminished renal catabolism of these biologically inactive fragments leads to their significant accumulation in serum.

Two commercial kits based on the two-site immunometric principle have recently become available that measure only intact PTH in serum (*1, 2*). In both kits, the "Allegro intact PTH" (Nichols Institute Diagnostics, San Juan Capistrano, CA 92675) and "N-tact PTH IRMA" (Incstar Corp., Stillwater, MN 55082), the first polyclonal antibody is specific for PTH 39-84, and is bound to a solid phase. Manufacturers of both kits claim that the capacity of this solid phase is adjusted to cope with the high concentrations of C-terminal and mid-molecule fragments often encountered in patients with severe or end-stage renal failure. Here we report a comparison of the two kits for their ability to measure only intact PTH serum from renal dialysis patients.

Pre-dialysis blood was collected from 12 patients who were undergoing long-term maintenance hemodialysis. Each serum was initially analyzed for PTH with the Incstar mid-molecule PTH kit; results ranged from 400 to 2600 pmol/L. Each serum was serially diluted (1:2, 1:4, 1:8) with zero standard supplied by each manufacturer. The undiluted and serially diluted sera were then assayed by both the Allegro and Incstar methods for intact PTH. The following tabulation shows the mean values measured by each method for the undiluted serum, and the mean results calculated for undiluted serum from the values obtained for each dilution.

	Intact PTH in serum, pmol/L (n = 12; mean ± SD)			
		Diluted[a]		
Method	Undiluted	1:2	1:4	1:8
Incstar	21.4 ± 7.3	24.5 ± 11.6	27.4 ± 13.3	33.1 ± 28.3
Allegro	33.2 ± 14.7	33.5 ± 16.0	33.5 ± 15.0	33.9 ± 15.2

[a] Calculated as measured result × dilution factor.

The Allegro intact PTH method yielded consistent values from each dilution, whereas those determined by the Incstar kit displayed very significant nonlinearity with dilution. For the Incstar method, the difference between the two intact PTH values obtained for each serum (value calculated from result for eightfold-diluted serum minus the result for undiluted serum) showed a strong positive correlation ($r = 0.61$, $P < 0.05$) with its respective mid-molecule PTH concentration. Such interference was not evident in the Allegro kit at the PTH concentrations we examined. Other studies, in which various amounts of synthetic PTH fragments have been added to kit standard

serum, have shown either significant (*1*) or no (*3*) interference. In contrast, our study applied the dilution technique for detecting interfering substances in patients' sera.

We conclude that the Incstar N-tact PTH kit is prone to significant negative interference by C-terminal and mid-molecule fragments in assays of PTH in serum from renal dialysis patients and should not be used in this diagnostic setting.

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Intra-Individual Variation of the Electrophoretic Serum Protein Fractions, *L. Juan-Pereira and X. Fuentes-Arderiu* (Servei de Bioquímica Clínica, Hospital de Bellvitge "Prínceps d'Espanya," Feixa Llarga s/n, 08907 L'Hospitalet del Llobregat, Barcelona, Spain)

We assessed the biological variation of the serum protein fractions, to obtain the analytical goals for the imprecision (CV_D) (*1*), the indices of individuality (r) between the intra-individual (CV_I) and the inter-individual (CV_G) variations (*2*), and the critical differences for two serial results to be significantly ($P < 0.05$) different (d) (*3*) for each of the serum protein fractions.

We studied 20 healthy volunteers (six men and 14 women, ages 24–70 y), blood being sampled once a month for a year. The serum protein fractions were determined by electrophoresis on cellulose acetate (Cellogel; Chemetron International Sales Headquarters, Milan, Italy), followed by staining with Amido Black (Merck, Darmstadt, F.R.G.). The stained and cleared cellulose acetate strips were then scanned at 525 nm in a densitometer (Super Cellomatic; Atom S.A., Barcelona, Spain). The samples were analyzed on the same day of sampling and the between-day imprecision (CV_A) was assessed by replicate analyses of 20 aliquots from a pool of sera stored at −20 °C.

The results, expressed in SI units:

	Mean	CV_A,%	CV_I,%	CV_G,%	CV_D,%	r	d
Albumin	0.58	6.1	4.1	5.1	2.0	1.4	0.12
α_1-Globulin	0.03	13.4	10.0	22.6	5.0	1.1	0.02
α_2-Globulin	0.09	7.5	10.4	12.7	5.2	1.0	0.03
β-Globulin	0.13	5.1	9.6	9.2	4.8	1.4	0.04
γ-Globulin	0.16	9.5	11.2	12.3	5.6	1.3	0.06

The biological variation of these electrophoretic fractions of serum has not been reported before. We derived the state of the art for the imprecision, calculating the 0.25 fractile of approximately 20 laboratories participating in a European quality-control scheme (Merz+Dade AG, Düdingen, Switzerland): albumin 2.6%, α_1-globulin 11.1%, α_2-globulin 8.1%, β-globulin 6.0%, and γ-globulin 6.0%. We did this to compare these data with the goals for the imprecision arising from biological variation. In any case, the imprecision we attained was less than the state of the art. It seems difficult to improve the precision, owing to the intrinsic characteristics of the technical procedure itself (*4*).

The biological variation of the serum protein fractions measured by more up-to-date methods should be studied. In this way, objective criteria would be available for the selection of an alternative to electrophoresis on cellulose acetate.

The indices of individuality for albumin and β-globulin are 1.4 (see the above tabulation), indicating that conventional population-based reference values are of clinical utility. For the other analytes r is <1.4, so it seems to be more useful to apply the individual reference values.

Assuming the homoscedasticity of the serum proteins, it is possible to apply the critical differences between two serial results to see if they are significantly ($P < 0.05$) different. The critical differences have been reported before (*5*), but only the analytical variability was considered; the contribution of the biological component to the total variation of the serum proteins was not considered.

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Impact of Acute Phase on Concentrations of Tissue Plasminogen Activator and Plasminogen Activator Inhibitor in Plasma after Deep-Vein Thrombosis or Open-Heart Surgery, *Jan-Håkan Jansson,[1] Bo Norberg,[2] and Torbjörn K. Nilsson[3,4]* (Depts. of Internal Medicine, Skellefteå Hospital[1] and Umeå University Hospital,[2] and Dept. of Clin. Chem.,[3] University Hospital, S-90185 Umeå, Sweden)

The clinical application of the fibrinolytic indicators in investigation and treatment of thromboembolic diseases might be confounded because tissue plasminogen activator (tPA) and plasminogen activator inhibitor (PAI-1) behave like acute-phase reactants, e.g., in the postoperative period (*1, 2*) and during endotoxin infusion (*3*). Our aim in this study was to define an appropriate time lapse after which measurement of these analytes would accurately reflect the individual's constitutional level of them.

Of all 258 patients attending the outpatient clinic of the Department of Internal Medicine, Umeå, for oral anticoagulant treatment, we selected for the present study 18 subjects who were started on treatment with warfarin in the acute phase after deep-vein thrombosis (n = 9) or

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