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evaluated. We cited this work by Galen et al., not in support of the exclusion of *all* enzyme tests, but rather to illustrate the exclusion of all of those tests being evaluated. Since Galen et al. chose to examine the efficacy of six enzyme assays commonly used in classifying patients with chest pain, they rightfully excluded all six from the diagnostic criteria. Our concern is specifically that studies should exclude the test(s) under evaluation and closely related tests from the diagnostic criteria. We recognize that this may result in difficulties in establishing the true diagnosis because, after elimination of these tests, the remaining parameters in a routine workup may be insufficient to make accurate diagnoses. In this event, the use of nonroutine or extraordinary means, tests, or procedures may be required for establishing the definitive diagnosis. To the extent that the diagnosis is not accurately and independently determined, the accuracy and objectivity of the evaluation is compromised and the conclusions may be biased.

Also, Ljungdahl et al. mention that, in a more recent study (*3*), they "reclassified the patient material for each single test to be evaluated by excluding the test under evaluation from the diagnostic criteria." While this approach seems appealing and has been used by others (*4*), it actually introduces bias. If each test is in turn excluded from the criteria and the patients reclassified for each test, then each test will be evaluated against differing criteria, with the "best" test being evaluated against the poorest criteria. Furthermore, because the criteria are varying, patients may be classified as AMI for one or more tests and as non-AMI for others. Thus, the various tests will not be examined under truly comparable conditions or circumstances.

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Markedly Increased Prostatic Acid Phosphatase as Measured in a Patient by a Monoclonal Antibody Method

To the Editor:

We wish to report a case of a patient with an extremely increased value for prostatic acid phosphatase (PAP, EC 3.1.3.2). This 73-year-old white man was being treated with diethylstilbestrol for carcinomatosis secondary to prostatic cancer. His serum PAP value was 11.6 mg/L (normal reference interval for males; <2.8 μg/L).

The "Tandem" PAP kit (Hybritech, Inc., San Diego, CA 92121) was used for the assays. This is a solid phase two-site immunoradiometric assay technique in which the test sample reacts simultaneously with radiolabeled monoclonal antibody and solid-phase monoclonal antibody. The bound counts per minute (cpm) are directly proportional to the concentration of PAP in the test sample. The patient's sample was initially assayed undiluted and gave bound cpm essentially equal to the highest standard provided (30 μg/L). The specimen was re-assayed, after dilution with the zero standard. Data are presented in Table 1.

We believe this to be the highest result for PAP yet reported. Note that neither the undiluted sample nor the threefold dilution gave the maximum bound counts, as would be expected with such high values. Although the assay has excess binding agent, there must have been considerable unbound PAP, especially in the undiluted and low-dilution specimens. This would result in a disproportionate amount of labeled antibody bound to the free PAP antigen, so that less than maximal counts were gotten with the undiluted specimen. A plateau of maximal counts was obtained beginning with the specimen diluted fivefold, and the PAP was quantitated by using the 500-fold dilution.

Even though fewer than maximal counts were obtained with the undiluted specimen, the counts were sufficiently high to alert us to the high PAP concentrations and the need to repeat the test with diluted sample. According to the manufacturer, the assay will be re-optimized by increasing the concentration of the labeled monoclonal antibody (personal communication, Hybritech, Inc.).

Table 1. Bound Counts/Min for PAP

Standard, μg/L	Av. cpm
1	2000
5	6748
10	11 952
20	20 710
30	28 849
Patient's serum	
Undiluted	32 500
Threefold diln.	50 617
Fivefold diln.	52 055
10-fold diln.	55 026
500-fold diln.	23 970

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Short-Term Variability of Ferritin Concentrations in Serum of Children with Severe Protein–Energy Malnutrition

To the Editor:

Serum ferritin (SF) assay has been widely used as an indicator of iron stores in normal subjects and in several disorders of iron metabolism (*1*, *2*). Nevertheless, the correlation between SF and storage iron is lost in several conditions, including liver disease, malignancies, and severe infection (*3*). We would like to address another possible cause of such variability, the marked changes in plasma volume and total plasma proteins during the early phase of the recovery from protein–energy malnutrition (PEM) in children. This concern is justified by the increasing use of SF in the diagnosis and follow-up of the anemia associated with PEM.

We studied 19 children, ages 12 to 56 months, admitted to our Clinical Research Center with a diagnosis of severe PEM of the edematous type (kwashiorkor and marasmic kwashiorkor). Blood was sampled at admission and on the seventh day of hospitalization. SF was determined by immunoradiometric assay (*4*) (Fer-Iron; Ramco Laboratories, Inc., Houston, TX 77093). Total plasma proteins were determined refractometrically. Also, a microhematocrit was obtained for each

sample. The results are shown in Table 1. Mean SF was 22.4 (SD 26.3) μg/L on admission and 26.0 (SD 30.4) μg/L on day 7. The average change between the two determinations was 3.6 (SD 12.6) μg/L. The largest difference between the two measurements was in Case 12, who increased his SF from 16 to 44 μg/L. We previously have used an empirical cutoff point of 30 μg/L to separate children with "low" or "normal" iron stores. With this criterion, only two of the present 19 children would have been reclassified as "normal," owing to the variability of SF between days 0 and 7. Although these two children (Cases 6 and 12) also showed a dramatic increase in total plasma proteins during the first week, this phenomenon is not clearly associated with the increase in SF. For example, patient 14, who showed the largest increase in plasma proteins, had identical SF values in both determinations. Some children also had mild episodes of upper respiratory tract infection or a positive urine culture during the first week of admission, but neither of these was associated with larger changes in SF.

There is a normal day-to-day variability in SF that also must be considered. Pilon et al. (*5*) studied 13 healthy adults during five weeks, and reported a day-to-day variability of around 15%; they used radioimmunoassay. On the other hand, Lipschitz et al. (*6*) compared the RIA with the IRMA (Ramco) kit, and found better reproducibility with the latter for samples from iron-deficient subjects.

In spite of their marked protein depletion, five of our 19 children had SF values at or above those considered normal for this age group (*7*), in agreement with experimental data (*8*) showing conservation of ferritin synthesis in response to iron administration in protein-deficient rats. Moreover, we found that the sequential changes in SF and plasma proteins throughout recovery from PEM follow independent patterns, the latter related to the overall repletion of the body protein pool, the former probably associated with the recovery of iron reserves.

We conclude that SF concentrations are fairly stable during the first week of treatment of severe PEM, in spite of the marked changes in intravascular volume and in protein metabolism that occur during this interval.

Table 1. Serum Ferritin, Hematocrit, and Total Plasma Protein Concentration in Severely Malnourished Children, on Admission and at the 7th Day of Hospitalization

	Serum ferritin, μg/L			Hematocrit, vol %			Plasma proteins, g/L		
Case	Day 0	Day 7	Δ	Day 0	Day 7	Δ	Day 0	Day 7	Δ
1	98	123	25	34	32	−2	43	53	10
2	11	29	18	36	31	−5	42	45	3
3	48	56	8	33	28	−5	40	45	5
4	0	2	2	35	32	−3	43	53	10
5	17	11	−6	41	37	−4	46	47	1
6	18	38	20	35	34	−1	34	50	16
7	2	12	10	16	17	1	37	44	7
8	8	5	−3	35	32	−3	41	46	5
9	6	13	7	15	10	−5	39	41	2
10	66	47	−19	36	30	−6	43	47	4
11	60	62	2	30	25	−5	40	43	3
12	16	44	28	29	30	1	37	50	13
13	5	7	2	34	30	−4	48	46	−2
14	7	6	−1	27	28	1	33	51	18
15	6	4	−2	35	32	−3	41	51	10
16	22	5	−17	31	28	−3	28	37	9
17	11	7	−4	34	33	−1	43	56	13
18	13	13	0	34	33	−1	38	46	8
19	12	10	−2	30	31	1	44	49	5
Mean	22.4	26.0	3.6	31.6	29.1	−2.5	40	47	7
(SD)	(26.3)	(30.4)	(12.6)	(6.5)	(6.2)	(2.3)	(5)	(5)	(5)

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Diagnostic Value of Sequential Readings with the Minolta Transcutaneous Bilirubinometer in Normal and Low-Birthweight Infants

To the Editor:

Several studies have demonstrated a correlation between readings with the Minolta transcutaneous bilirubinometer (Tc-BM) and serum bilirubin in newborns of various racial groups (*1–3*). Thus this instrument has been advocated as an alternative to serum bilirubin determinations (*1*), but little attention has been paid to interpretation of sequential measurements on newborns with the Tc-BM. We have evaluated the diagnostic value of sequential readings and we propose guidelines for the interpretation and use of information given by the Tc-BM. The study was conducted on newborns grouped by body weight and presence or absence of phototherapy.

The Minolta Tc-BM was used as recommended by the manufacturer (distributed by Narco Scientific, 640 Petrolia Rd., Downsview, Ontario, Canada, L3J 2W3), and each reading was correlated wih serum total bilirubin as measured by a Jendrassik–Grof procedure (American Monitor Corp., Indianapolis, IN 46268).

The population we studied included only white newborns. All Tc-BM readings were performed on the forehead of the newborns. For patients who were receiving phototherapy, these readings were made on the region covered by the eye mask. For the benefit of uniformity, three readings per newborn, with or without phototherapy, were compared with the corresponding results for total bilirubin. When more than three values were available for a newborn, we used the first, middle, and last values. The regression equation, the standard deviation of the slope, and the intercept were calculated. We used the