

sensitivity TSH assay is one in which sera from clinically hyperthyroid patients invariably give results which are more than three log standard deviations below the mean value found in sera from a healthy euthyroid population" (1).

The mean value for the euthyroid population was 1.60 milli-int. units/L. After a natural-log transformation, the mean and SD were 0.3207 and 0.5666, respectively. The corresponding antilog to three log standard deviations below the log mean of a healthy euthyroid population equals a TSH concentration of 0.25 milli-int. unit/L.

Of the 63 hyperthyroid patients' specimens analyzed, 62 tested 0.25 milli-int. unit/L or less. The result for one hyperthyroid patient's specimen was 0.27 milli-int. unit/L. However, the lowest value for the euthyroid population was 0.29 milli-int. unit/L, demonstrating complete differentiation.

The second definition (2) involves constructing a precision profile to determine the TSH dose at which CVs are 10% and 15%. Sixteen serum pools were run in triplicate in 10 assays, representing a total of 30 points for each pool. A CV of 15% and a CV of 10% were seen for TSH values of 0.19 and 0.40 milli-int. unit/L, respectively.

The second definition (2) recommends that TSH assays can "justifiably be called 'sensitive' and deserve further clinical trials in hyperthyroid patients if, and only if, the 'lower limit of quantitative measurement' falls clearly below the normal range." Therefore, the working sensitivity of the mab TSH assay is 0.19 milli-int. unit/L, clearly below the euthyroid lower limit cutoff of 0.3 milli-int. unit/L.

In summary, Ciba Corning Diagnostics' Monoclonal TSH Assay does, according to these two definitions, qualify as a highly sensitive TSH assay.

#### References

1. Revised nomenclature for tests of thyroid hormones and thyroid-related proteins in serum. *J Clin Endocrinol Metab* 1987;64:1089-94 [reprinted in *Clin Chem* 1987;33:2114-9, this issue].
2. Bayer MF. Performance criteria for appropriate characterization of "(highly) sensitive" thyrotropin assays [Letter]. *Clin Chem* 1987;33:630-1.

**Individual Variations of Carcinoembryonic Antigen (CEA) in Serum of Healthy Subjects, W. Riesen,<sup>1</sup> A. Ch. Kessler,<sup>2</sup> and V. Ehrhard<sup>2</sup>** (<sup>1</sup> Universität Bern, Institut für klinisch-experimentelle Tumorforschung, Tiefenauspital, CH-3004 Bern, Switzerland; and <sup>2</sup> Boehringer Mannheim GmbH, D-6800 Mannheim 31, F.R.G.)

CEA is now the most widely used indicator for a variety of malignancies. Usually the course of the disease is assessed by following the concentration of this tumor marker for a long time. Interpretation of such data would be facilitated by having an estimate of the biological variability of CEA with time in healthy subjects. Opinions in this field are inconsistent, so we measured serially the values for CEA in a number of ostensibly healthy subjects. The assay used was a solid-phase enzyme immunoassay (Enzymun-Test® CEA; Boehringer Mannheim GmbH, F.R.G.), used according to the instructions of the manufacturer. Samples were taken at intervals of one or two months, incorporated into the daily routine workload of the laboratory and analyzed in dupli-

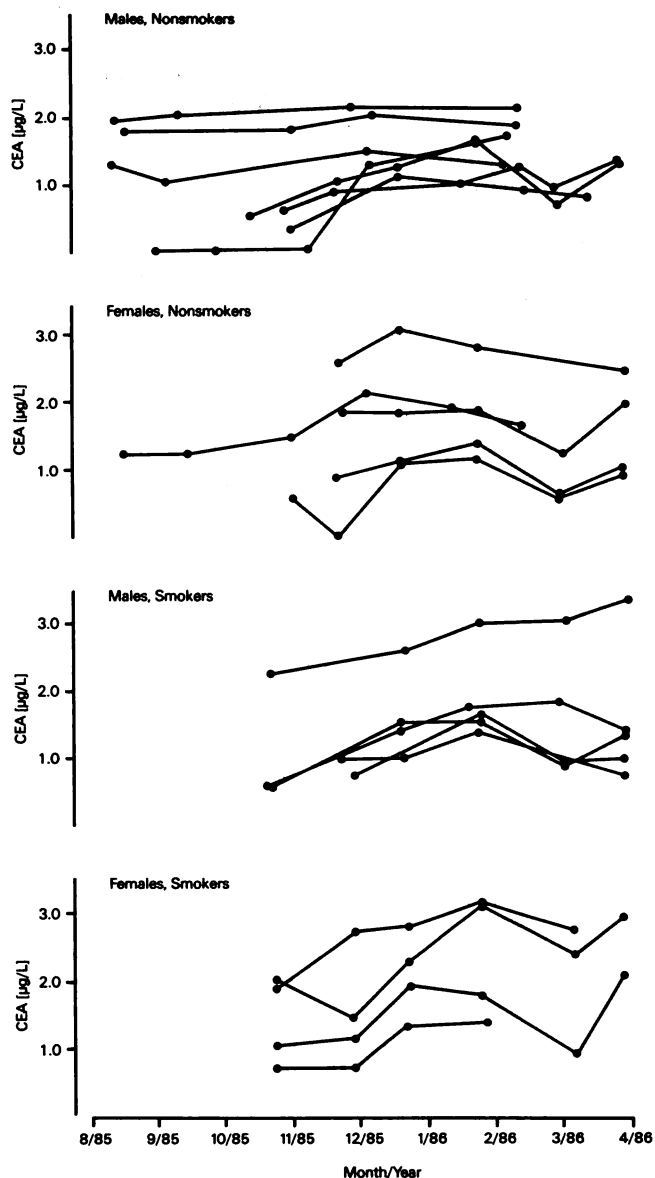


Fig. 1. CEA concentrations in serial samples from ostensibly healthy subjects, and effects of sex and smoking status

cate with the reagents of the lot currently being used. From the data depicted in Figure 1 it appears that the normal biological variability of CEA is lower than this assay's imprecision (*J Clin Chem Clin Biochem* 1987;25:53-9). The results presented here make it reasonable to assume that any pronounced change in CEA with time can be taken as a strong indication of a pathological process.

**An Emergency Test for Fetal Lung Maturity: OD 650 or Amniostat-FLM?** *J. C. McCulloch and D. Mendelsohn* (Dept. of Chem. Pathol., South African Institute for Med. Res., Hospital Street, P.O. Box 1038; and the Univ. of the Witwatersrand Med. School, Johannesburg, R.S.A.)

During our evaluation of an immunological assay for phosphatidylglycerol (A-FLM; Hana Biologics, Berkeley, CA) we introduced yet another test for potential emergency use, the "OD 650." Results of the two tests were compared

with those of our established routine profile: L/S ratio (1), phosphatidylglycerol by one-dimensional thin-layer chromatography (TLC-PG), and kit enzymatic assay of lecithin (Boehringer Mannheim GmbH, Mannheim, F.R.G.).

We adopted the suggestion (2) that an absorbance at 650 nm of <0.1 predicts fetal lung maturity and a result of >0.2 predicts maturity. The L/S ratio was considered to represent maturity when it exceeded 4, and the lecithin assay predicted maturity at concentrations >70  $\mu\text{mol/L}$ . The presence of detectable phosphatidylglycerol by either method was taken to indicate maturity.

Our method comparisons for 183 amniotic fluid specimens generally showed acceptable concurrence (range 66 to 91%) with regard to fetal lung maturity or immaturity. The following tabulation shows that OD 650 had the highest mean concurrence:

	TLC-PG	Lecithin	L/S ratio	OD 650	A-FLM
TLC-PG	—	73	66	84	81
Lecithin	73	—	83	91	84
L/S ratio	66	83	—	84	79
OD 650	84	91	84	—	91
A-FLM	81	84	79	91	—
Mean concurrence	76	83	78	88	84

A clinical trial involved 106 neonates whose delivery followed within three days of amniocentesis. There were 11 cases of respiratory distress in this group. Retrospectively from a clinical predictive point of view the most satisfactory test was OD 650 with a predictive value of 100% for a mature result and 80% for an immature result. For enzymatic lecithin the corresponding figures were 100% and 70%; for L/S ratio 97% and 50%; for TLC-PG 97% and 50%; and for A-FLM 99% and 26%.

Our results suggest (a) that an OD 650 value >0.2 predicts fetal lung maturity, (b) an OD 650 value <0.1 has a high probability of predicting respiratory immaturity, and (c) intermediate results, between 0.1 and 0.2, which composed 29% of our samples, had only a 6% risk of being associated with respiratory immaturity. On the basis of these results OD 650 is established as part of our routine test profile. We see no place for the A-FLM test for phosphatidylglycerol in our service.

#### References

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**Improved Jaffé Creatinine Reagent for the "Parallel" Analyzer,** G. A. Mackay,<sup>1</sup> G. I. Goodall,<sup>1</sup> J. Woods,<sup>2</sup> and V. H. Young<sup>1</sup> (<sup>1</sup> Dept of Biochem, Austin Hospital, Heidelberg, Victoria, Australia 3084; and <sup>2</sup> American Monitor Corp., Melbourne)

Our laboratory recently had a Parallel Analyzer (American Monitor Corp., Indianapolis, IN 46268) installed. Creatinine values for patients with bilirubin values >200  $\mu\text{mol/L}$  were up to 80% less than those obtained with an "Astra 8" (Beckman Instruments, Fullerton, CA 92634). Osberg and Hammond (1) have shown that addition of bilirubin to give concentrations up to 250  $\mu\text{mol/L}$  resulted in no interference with creatinine as measured in the Astra.

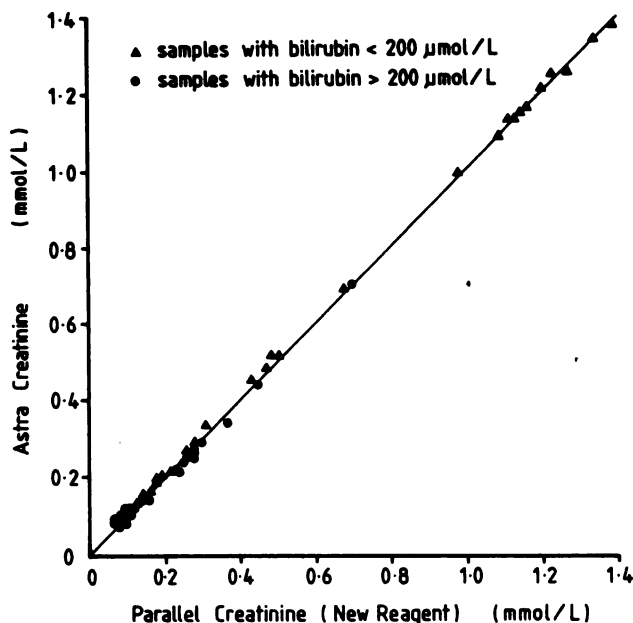


Fig. 1. Astra 8 creatinine results vs Parallel results with proposed formulation of Jaffé reagent

In the Parallel and Astra analyzers a kinetic Jaffé reaction is used, but reagent composition and reaction timings differ (2, 3). The Parallel reagent consists of 9 mmol/L picrate, 90 mmol/L sodium hydroxide, dimethyl sulfoxide, a non-reactive surfactant, and a stabilizer. The modified Beckman Astra reagent (4) consists of 9 mmol/L picrate, 190 mmol/L sodium hydroxide, 16 g/L sodium dodecyl sulfate (SDS), borate and phosphate buffers, and potassium ferricyanide. The Astra creatinine reading is taken at 25.6 s. The Parallel Analyzer takes readings at 75 and 225 s.

We tried various formulations of these components in the Parallel analyzer and found that substituting 16 g/L SDS for dimethyl sulfoxide and omitting the stabilizer and surfactant in the Parallel creatinine reagent resulted in a reagent that shows no interference from bilirubin in concentrations up to 800  $\mu\text{mol/L}$  in the Parallel analyzer—and also is free of interference from acetoacetate, glucose, urea, ascorbate, and pyruvate. The standard curve is linear up to at least 1.5 mmol/L, and the reagent is stable for at least three months at room temperature.

Results obtained on using the new reagent compare favorably with those from the Astra ( $n = 84$ ,  $r = 0.9995$ , slope = 1.0005, intercept = -0.0003) (Figure 1).

Between-run precision data were as follows: for 0.13 mmol/L, the CV = 3.7%; for 0.54 mmol/L, the CV = 1.0%.

The new reagent is used routinely in our laboratory. This more specific reagent should prove adaptable to many manual and automated creatinine assays.

#### References

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