was required to help with problems such as erroneous calibration. The manufacturer claimed that the direct costs of POCT (50 pence/sample for 50 samples/day or 35 pence/sample for 100 samples/day) were similar to the costs of central laboratory testing (38 pence/sample); however, there was no transferable saving because of the central laboratory funding structure, and there was a substantial additional capital cost. We concluded that POCT in our ED was not an efficient use of resources.

Our findings support those of Parvin et al. (2), who considered it unlikely that routine POCT in a large ED would by itself affect patients' length of stay. Similarly, Kendall et al. (3) found no effect of POCT on clinical outcomes or the time patients spent in the department because additional care for most patients was limited by the availability of inpatient beds. They did find that POCT reduced the time taken to make patient management decisions that were dependent on the results of blood tests. We agree that more evidence is needed on therapeutic outcomes to justify the use of POCT with limited funding.

**References**


**Carbamylated Hemoglobin Interference in Glycohemoglobin Assays**

*To the Editor:*

Glycohemoglobin is widely accepted as a valuable indicator for long-term diabetic control (1). The in vivo reaction of hemoglobin with urea-derived isocyanate and the possible interference of the resulting carbamylated hemoglobin in uremic patients have been described (2). Since our earlier studies (3, 4), conflicting results have been reported (5–7) and methods have been modified or newly introduced.

We recently revisited carbamylated hemoglobin as part of the educational program of the European Reference Laboratory for Glycohemoglobin (ERL). We investigated the interference of carbamylated hemoglobin in uremic patients by comparing HbA1c results in lyophilized specimens from a uremic patient and a nonuremic volunteer, both being nondiabetic, and the possible interference of the resulting carbamylated hemoglobin in uremic patients have been described (2). Since our earlier studies (3, 4), conflicting results have been reported (5–7) and methods have been modified or newly introduced.

We recently revisited carbamylated hemoglobin as part of the educational program of the European Reference Laboratory for Glycohemoglobin (ERL). We investigated the interference of carbamylated hemoglobin in uremic patients and a nonuremic volunteer, both being nondiabetic, in the 1998 ERL program. The first sample was prepared from the blood of a 50-year-old man with a mean urea during the preceding month of 27.9 mmol/L. According to a previous study (3), which concluded that 0.063% carbamylated hemoglobin is

**Fig. 1. Critical path analysis illustrating 1-night median data during trial period of POCT vs testing at central laboratory.**

Critical paths determined by summation. CXR, chest x-ray; ECG, electrocardiogram.
associated with each mmol/L of urea, a carbamylated Hb percentage of 27.9 ± 0.063% = 1.8% was expected. Using capillary electrophoresis, our group separated carbamylated hemoglobin from HbA1c (8), and a value of 2.0% was found in this specimen. The second sample was chosen on the basis of having an equal HbA1c percentage as the first sample and a carbamylated hemoglobin concentration of 0.3%, which is within the health-related reference range (with both HbA1c and carbamylated hemoglobin measured with National Glycohemoglobin Standardization Program-certified capillary electrophoresis).

This specimen was analyzed by 24 laboratories of the ERL program (in 17 countries) using 14 methods, and the results were compared with those for the sample from the nonuremic volunteer (Table 1). The results on the two samples agreed within 0.5% by immunologic, affinity chromatographic, capillary electrophoresis, and IMx methods. All HPLC methods based on ion-exchange chromatography showed higher HbA1c percentages in the sample of the uremic patient. The mean difference for all 21 HPLC users was 1.6%, quite near the calculated value of 1.8% and the observed value of 2.0% for carbamylated hemoglobin with capillary electrophoresis. This is not entirely unexpected because urea reacts with the hemoglobin molecule at the same site as does glucose, and the isoelectric point of carbamylated hemoglobin is thus similar to that of HbA1c. As a consequence carbamylated hemoglobin might be assayed as HbA1c in methods based on differences in electrical charge. In the immunoassays (+0.1%) and capillary electrophoresis (−0.1%), hardly any difference was seen. Interestingly, HPLC based on affinity chromatography (+0.5%) and Abbott IMx (+0.4%) showed a small but significant difference. Conclusions, based on results from a single sample, should be made with caution: even between two nonbiased methods differences up to 1% might occur because of scatter in individual patients. The mean difference of 1.6% as seen with ion-exchange methods seems too large to be explained by individual scatter, but the 0.5% seen with affinity methods might be attributed to this phenomenon. The persistence of carbamylated hemoglobin interference will be investigated in the next ERL program with a specimen from another uremic patient. An additional problem, although not directly related to carbamylated hemoglobin, is the frequent occurrence of shortened erythrocyte life-span in renal failure, which might obscure correct interpretation of HbA1c outcome.

We believe that carbamylated hemoglobin gives rise to falsely high HbA1c in all HPLC methods based on ion-exchange chromatography.

References
Usefulness of Procalcitonin in Neonates at Risk for Infection

To the Editor:

We are very interested in the report by Sachse et al. (1) on procalcitonin (PCT) variations in the neonatal period. This report confirms and extends previous work on the daily variations of PCT during the first days of life in noninfected newborn infants (2, 3). We agree that PCT could be a useful marker for the presence, course, and prognosis of bacterial infection, particularly in newborns hospitalized with a risk factor for infection (such as an increase in the mother’s body temperature during delivery, premature rupture of membranes, vaginal colonization by group B streptococcus, and other factors). In this context, prophylactic antibiotic therapy is started during labor and if clinical signs of infection are present at delivery, antibiotics are continued. Thus, the diagnosis of infection cannot be confirmed by culture because this preventive therapy is responsible for the negativity of bacteriological tests (blood and cerebrospinal fluid cultures).

We present additional data on PCT values obtained in 52 neonates hospitalized with a risk factor for infection. All mothers received a prophylactic antibiotic (Ampicillin®), and all samples were negative by bacteriological tests. Two groups were defined on the basis of health status. The first group (n = 44) comprised newborn infants with a risk factor for infection without clinical signs of infection. The second group (n = 8) comprised newborn infants with a risk factor for infection and clinical signs of infection at birth (bradycardia, apnea, hypotension, microcirculation impairment, changes of skin coloration, or an increase of the neonate’s body temperature).

The blood samples were obtained at 24 and 72 h of life. PCT was determined using an immunoluminometric assay (Brahms Diagnostica). The PCT concentrations (3.5 ± 0.5 μg/L) in the group of newborn infants without clinical signs of infection (Table 1) were similar to those published elsewhere (1–3). In contrast, in the second group a significant increase of PCT was observed on the first day of life (58.2 ± 7.1 μg/L). Nevertheless, these values were lower than our previous values described in materno-fetal infection, e.g., 162 ± 32 μg/L (2), but higher than the physiological peak reported by Sachse et al. (1) and by our group (2). In the second group, PCT concentrations decreased on the third day of life. Thus, increased PCT represents a biological marker of maternal-fetal infection, the negativity of bacteriological samples being a reflection of the efficacy of the early antibiotic prophylaxis.

In conclusion, even with the existence of a physiological peak, PCT is useful in the diagnosis and monitoring of neonates at risk of infection, particularly when the bacteriological samples are negative. Additional data are needed to document the value of PCT measurements for reducing the need for invasive collection of samples for bacteriological testing and for reducing the use/abuse of antibiotics.

| Table 1. Serum PCT concentrations (μg/L) during the first days of life obtained in 52 neonates hospitalized for a risk factor for infection with or without clinical signs of infection. |
|-----------------|-----------------|-----------------|
| **Patients**    | **24 h of life**| **72 h of life**|
| **Group 1 (n = 44); without clinical signs of infection** | Mean ± SE | 3.5 ± 0.5 | 0.57 ± 0.23 |
| | Median | 1.7 | 0.5 | |
| | Range | 0.4–16 | 0.1–2.1 | |
| **Group 2 (n = 8); with clinical signs of infection** | Mean ± SE | 58.2 ± 7.1a | 8.3 ± 2.5a |
| | Median | 60 | 6.5 | |
| | Range | 23–111 | 1–19 | |

*Significance of results between group 1 and group 2; P < 0.001, Mann–Whitney test.