homeostasis in the newborn is extremely important to good patient care in the neonatal intensive care setting, and the laboratory is frequently challenged to provide a more rapid and sensitive means of determining blood glucose in the hypoglycemic infant (1). Recently, several point-of-care testing instruments have been developed that allow for on-site glucose testing at the low end of the dynamic range of glucose measurements (2). We recently evaluated the Precision-G System by MediSense, which can determine glucose on a 5-μL blood specimen in 20 s at the bedside with a dynamic range that extends to 1.11 mmol/L (20 mg/dL). Seventy-four consecutive blood samples from the neonatal unit were collected by heelstick into lithium heparin capillary tubes, and glucose was determined simultaneously on the 950 analyzer and the Precision-G System. The neonatal population we studied demonstrated the usual range of normal to high hematocrit concentrations in a neonatal unit by the Precision-G (y-axis) vs the Vitros 950 (x-axis).

Fig. 1. Scattergram comparing blood glucose analysis of 74 consecutive blood samples from our neonatal unit by the Precision-G (y-axis) vs the Vitros 950 (x-axis).

Values obtained with the Precision-G and the Vitros 950 (Fig. 1) revealed a correlation coefficient of 0.993 (S_{y|x} = 0.43 mmol/L), an intercept = -0.053 (± 0.002) mmol/L, and a slope of 0.946 (± 0.051). Although the number of samples in the true hypoglycemic range was rather limited, the results from 14 subjects with glucose values obtained with the Precision-G results below 2.22 mmol/L (40 mg/dL) fell on the regression line. Overall, there was a slight negative systematic difference observed with the Precision-G results that averaged 0.31 mmol/L; differences in the analytical methods and the use of whole blood vs plasma sample most likely account for this difference. This slight difference, however, should have little influence on the neonatologist’s clinical decision regarding the detection of hypoglycemia. Between-run imprecision (CV) with the Precision-G using Abbott MediSense control material at 1.11 mmol/L (20 mg/dL) was 8% (n = 15). It is our impression from these results that the Precision-G System can be used effectively to determine low blood glucose concentrations in a neonatal unit.

References

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To the Editor:

APOE genotyping to identify subjects with the E4 allele is helpful in the diagnosis of Alzheimer disease when used together with clinical criteria (1). The most common APOE genotyping method involves digestion of a 244-bp PCR-amplified fragment of APOE exon 4 followed by digestion with endonuclease HhaI (2). The digestion creates a characteristic pattern of DNA bands in electrophoresis gels for each of the three common APOE alleles (E4, E3, and E2) and thus for the six common APOE genotypes (E4/E4, E3/E3, E2/E2, E4/E3, E3/E2, and E4/E2) (2). However, there are four additional HhaI recognition sites within the 244-bp fragment that is amplified by this method, and the fragment also harbors several sites that differ from the HhaI recognition sequence (GGG/C) by a single nucleotide (2).

In the course of >2000 APOE genotyping reactions, we have observed two individuals who had patterns of HhaI restriction fragments that were distinct from any that could have resulted from the common APOE genotypes (Fig. 1). DNA sequencing of these two individuals revealed that each was heterozygous for a different rare APOE mutation,
resulting from the E4/3, E3/3, and E4/2 genotypes, respectively. Lanes 6 and 7 each show an atypical HhaI

has been estimated to be as

http://www.medicaljournals.ac.uk/annals/doi/10.1136/annrheumdis.54.11.1038

Lanes 3–5 show the typical fragment patterns of a HhaI recognition site in codon 136. For the subject in lane 6, a C

(http://www.idealibrary.com/article/1548524709/0) 3 bp. DNA sequencing showed that in both cases the 109-bp fragment resulted from the loss

These potential problems could be circumvented by the use of an APOE genotyping method that is limited only to the detection of the C→G change underlying the R/C112 amino acid polymorphism underlying the E4 allele (4), thus eliminating the possibility of detecting any other APOE sequence changes.

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References


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To the Editor:

Dr. Hegele’s finding of unique disease-causing mutations in the APOE gene during routine genotyping for Alzheimer disease highlights the continuing need for broad patient-oriented clinical observation and intervention as genetic discoveries and tests move from the research laboratory into clinical use. This type of discovery, made in the course of clinical testing, can be stifled by the monopolization of testing services enabled by the exclusive licensing of genetic testing patents (1). Indeed, Dr. Hegele admits in his letter to performing more than 2000 tests, and his performance of these tests may well infringe a Canadian patent sought by Duke University on APOE testing. Laboratorians in the US are prevented from making similar discoveries because of the exclusive license on the test granted by Duke to Athena Diagnostics. The fear of being sued might also lead clinical laboratorians not to publish such findings, which is a foreseeable and unfortunate result of patents on medical processes such as tests, and which would be antithetical to medical and scientific norms.

Perhaps more importantly, Dr. Hegele notes the importance of working with informed patients (and perhaps involved family members) to determine the proper scope of testing to be performed. This example of the uncertainty and continuing research nature of clinical discovery about the role of genetic mutations in Alzheimer disease also supports the assertion that a patent-based monopoly on clinical testing services unreasonably interferes with both patient care and science. This will likely become more of a problem as tests move into clinical use for the rapidly growing list of known disease genes.