

LETTER TO THE EDITOR

Alpha-1-Fetoprotein (AFP) Measurements and the High-Dose Hook Effect

THOMAS BERTSCH¹, CORNELIUS BOLLHEIMER², URSULA HOFFMANN³,
HANS-JÜRGEN HEPPNER⁴, JAKOB TRIEBEL¹, CORNEL SIEBER², MICHAEL CHRIST⁵,
ANNE-MARIE DUPUY⁶, JEAN-PAUL CRISTOL⁶, PAUL KENNY⁷

¹*Institut für Klinische Chemie, Laboratoriumsmedizin und Transfusionsmedizin-Zentrallaboratorium, Klinikum Nürnberg, Germany*

²*Klinik für Allgemeine Innere Medizin und Geriatrie, Krankenhaus der Barmherzigen Brüder Regensburg,*

Lehrstuhl für Innere Medizin-Geriatrie Universität Erlangen-Nürnberg, Germany

³*I. Medizinische Klinik, Universitätsmedizin Mannheim, Germany*

⁴*Klinik für Geriatrie, Helios Klinikum Schwelm, Lehrstuhl für Geriatrie der Universität Witten-Herdecke, Germany*

⁵*Klinik für Notfallmedizin und Internistische Intensivmedizin, Klinikum Nürnberg, Germany*

⁶*Department de Biochimie Hopital Lapeyronie Centre Hospitalier Universitaire, Montpellier, France*

⁷*KKPD GbR, München, Germany*

(Clin. Lab. 2014;60:1585-1586. DOI: 10.7754/Clin.Lab.2014.140122)

TO THE EDITOR

Three years ago we published the results of an international proficiency study regarding Alpha-1-Fetoprotein (AFP) measurement on different test systems [1]. After discussions between laboratory experts and experts in internal medicine we came to the conclusion that we should report about an additional phenomenon that can occur in AFP measurements on different test systems: The high-dose hook effect. The hook effect is most likely to occur when a 1-step assay is used. If unusually high concentrations of analyte are present (more than that of available antibody binding sites - the hook threshold) there is competition for these between the excess of free analyte and already-bound, analyte-labelled antibody complexes. Due to this excess, free analyte is more likely to become bound and consequently, when results are obtained, it shows an erroneously low concentration. A more convenient solution would be to use a 2-step assay. Unlike a 1-step assay, where all reagents are added simultaneously, in a 2-step assay, the analyte is added and then washed before the labelled antibody is introduced. This prevents the occurrence of excess analyte solely binding the labelled antibody, giving a true response.

To demonstrate the hook effect in 1-step and 2-step assays, we performed dilution experiments on the Elecsys 2010 (1-step assay; Roche Diagnostics, Mannheim, Germany), Centaur (1-step assay; Siemens Healthcare

Diagnostics, Eschborn, Germany), and AU 3000i (2-step assay; Olympus) with an AFP stock solution (Scipac, Kent, England). The AU 3000i, which showed very good performance data [2,3], was withdrawn from the diagnostic market after the merger of Olympus with Beckman Coulter. We could clearly demonstrate the hook effect in the two 1-step immunoassay systems and the absence of this effect in the 2-step AU 3000i immunoassay system (Figure 1). High-dose hook effect is an inconvenient and unpredictable phenomenon, which can give rise to costly, potentially fatal, false negative results [4]. This is usually due to the use of a 1-step assay. Using a 2-step assay can eliminate the problem. In laboratories where 1-step assays are used the laboratory staff as well as the clinicians should always keep the high-dose hook effect in mind, especially when there is a discrepancy between the clinical finding and the expected laboratory result. This is also a clear plea for a close communication between laboratory experts and clinicians.

Declaration of Interest:

The authors declare no conflict of interests.

Letter to the Editor accepted January 25, 2014

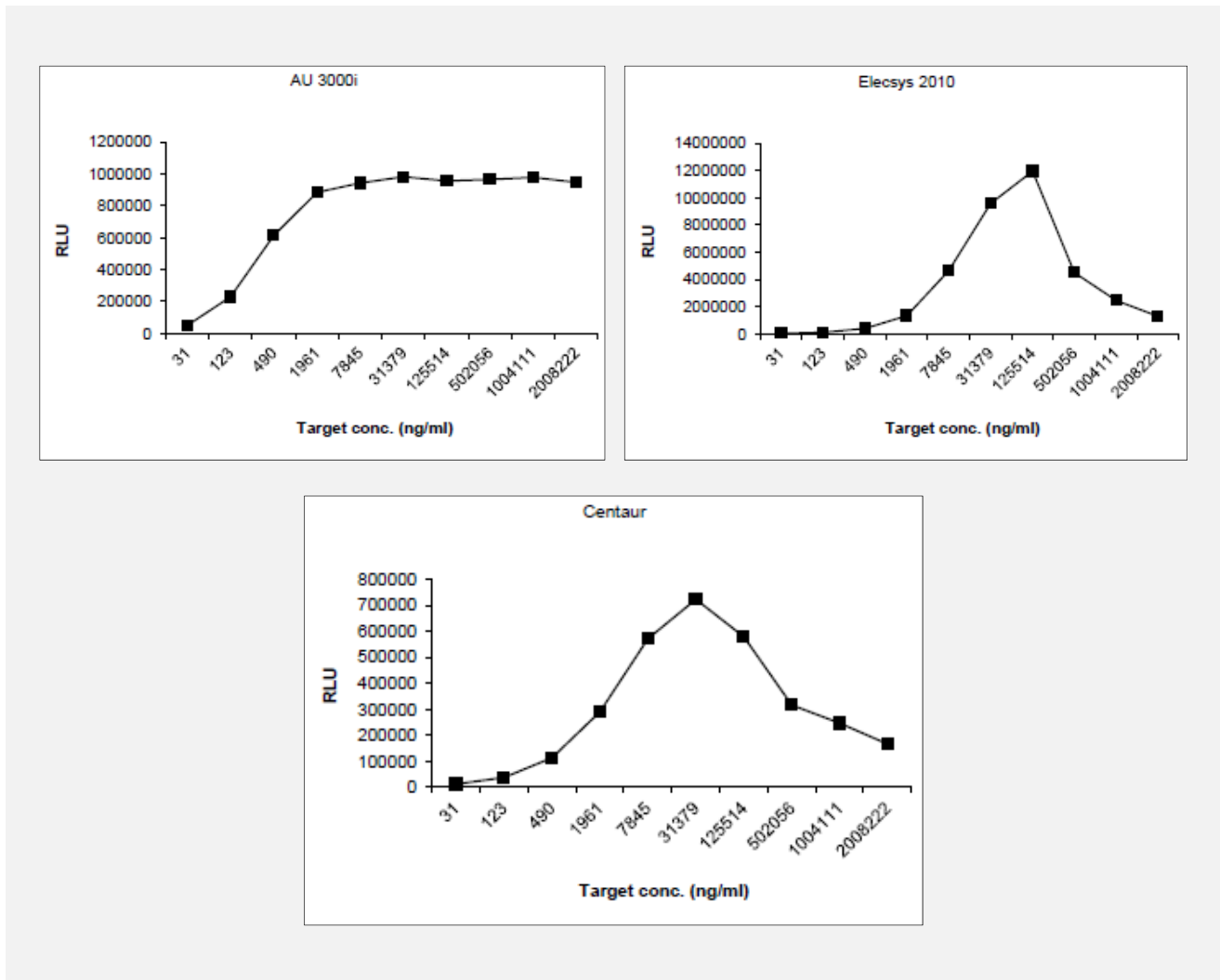


Figure 1. Demonstration of the high-dose hook effect in AFP measurements in three immunoassay systems. RLU = Relative Light Units.

References:

1. Oremek GM, Oertl A, Bertsch T, et al. Alpha-1-Fetoprotein (AFP): International proficiency study with different test systems. *Clin Lab* 2011;57:669-75.
2. Bertsch T, Aschenneller C, Herzog V, et al. A multicenter assessment of the analytical performance of the routine thyroid panel on the Olympus 3000i immunoassay system. *Clin Lab* 2009;55:447-58.
3. Bargnoux AS, Badiou S, Bertsch T, et al. Multicenter evaluation of workflow performance on the new Olympus AU 3000i. *Clin Lab* 2009;55:459-64.
4. Jassam N, Jones CM, Briscoe T, Homer JH. The hook effect: a need for constant vigilance. *Ann Clin Biochem* 2006;43:314-7.

Correspondence:

Prof. Dr. Thomas Bertsch
 Institut für Klinische Chemie
 Laboratoriumsmedizin und
 Transfusionsmedizin-Zentrallaboratorium
 Klinikum Nürnberg
 Prof. Ernst-Nathan-Strasse 1
 D-90419 Nürnberg, Deutschland
 Email: thomas.bertsch@klinikum-nuernberg.de