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LETTER TO THE EDITOR: MEASURED VALUES INCOMPATIBLE WITH HUMAN LIFE

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INTRODUCTION

To the Editor,

In the last decades, systems for quality control and improvement of measured values have been widely developed and implemented in the clinical laboratory. Thus, errors of any kind committed in clinical laboratories at any stage of the measurement process have declined substantially (1).

There are evidences that in the clinical laboratory these errors mainly occur at the pre-analytical and post-analytical steps of the total analytical process (1). The adoption of standards of quality such as ISO 9001:2008 (2) or, better, ISO 15189:2007 (3) —a specific document on technical competence in clinical laboratories— are actually cornerstones for trying to reach the excellence in the practice of clinical laboratory sciences. This excellence is directly translated into an improvement of the clinical laboratory information provided to the clinician and, consequently, an improvement of the clinical decision making process.

However, sometimes we can find clinical laboratory information in which although all steps of the analytical process have been exhaustivelly controlled, the information seems to be not reliable. This could be the case when a very extreme biological quantity value is found in a patient. Accordingly, it might be of interest, from a clinical laboratory point of view, to know those measured values which, being extremely high or low ones, have been obtained in the absence of performance abnormalities of the measuring system and would indicate that an error has occurred at any phase of the measurement process. Such an extreme measured value must be reviewed by professionals of clinical laboratory. But, what would it mean when an apparently impossible measured value has been found, and there is no evidence of error at any phase of the measurement process?

A measured value from a patient alive is really clinically impossible when it is not compatible with human life. Thus, when focusing on these apparently impossible values, the idea 'measured values incompatible with human life' easily arise in our mind. Unfortunately, for most biological quantities the information available on this topic is extremely rare and, consequently, it is very difficult to find publications regarding this issue. Moreover, in the few references found, the studies do not explain the experimental design, it is not detailed enough to assure its reliability.

Table 1. Published values incompatible with human life for some biological quantities.

Quantity[1]	Values incompatible with human live	Reference
P—Chloride; subst.c.	< 65 and > 138 mmol/L	**4**
P—Ethanol; subst.c.	> 97.6 mmol/L	**5**
Pt—Plasma; pH	< 6.8 and > 7.8	**6**
P—Potassium ion; subst.c.	< 1.3 and > 9.0 mmol/L	**4**
P—Sodium ion; subst.c.	< 100 and >191 mmol/L	**4**

[1] Quantities are described according to IFCC and IUPAC recommendations (13); "P" means blood plasma, "Pt" means patient, and "subst.c." means substance concentration.

In Table 1 there are few examples of publications on this kind of values (4-6) Despite the importance of these works, their results must be taken into account with caution; in Table 1, we can see an example. In the work of Vogt and Oesterle (4) a concentration of sodium ion in plasma lower than 100 mmol/L is considered incompatible with human life. Is this incompatibility verifiable? Hardly. Firstly, we will never be able to reproduce the exact conditions in which was found this measured value and, secondly, some publication can be found refusing this measured value as incompatible with human life. In a recent publication, concentration of sodium ion in plasma in a schizophrenic potomaniac patient was only 95 mmol/L (7). This patient was alive with this concentration of sodium ion in plasma and survived after electrolyte administration. There are only conclusive evidences of measured values incompatible with human life when the studies deal with absolute deficiency of essential components for human life, such as homozygous antithrombin deficiencies (8), for example. In the other hand, in toxicology, several concepts related to measured values incompatible with life in non-human populations have been defined: absolute lethal concentration (LC100), median lethal concentration (LC50) and minimum lethal concentration (LCmin) (9). However, for obvious reasons, this kind of concepts must not be applied to humans.

It could be of interest to set a discriminant value to decide when a measured values is non attributable to an alive human, but it is not an easy issue. Firstly, it is well known the amazing adaptability of humans to external and stress situations, as seen in studies dealing with physiological adaptation to extreme stress situations, as low oxygen partial pressure in extreme altitudes (10). Secondly, worldwide metrological harmonization has only been achieved for the measurement of very few biological quantities, so the measured values presumptively incompatible with human life obtained by one laboratory could not be verified by other laboratories. And, thirdly, and maybe the most important, serious ethical dilemmas arise in designing specific models to verify the most extreme measured value of any biological property that could be assumed as compatible with human life.

Thus, a deep sight into this topic provides the conclusion that, for any biological quantity, it is not possible to set a limit which clearly define a distinction between measured values compatible or non compatible with human life due to the intrinsic ethical and methodological limitations.

Probably, an unlikelyhood limit is the best surrogate for a value incompatible with human life. An 'unlikelyhood limit' is defined as a «measured value with a very low probability of belonging to a patient» (11). This way, it can be set, using statistical tools, an interval of measured values, which limits are defined by fractiles that exclude a defined fraction of laboratory measured values obtained and validated during a defined period of time (12).

All about measured values incompatible with human life is interesting in biological anthropology, health care sciences, in general, and clinical laboratory sciences, in particular. However, it is a complex issue, and some questions arise from the ambiguity and complexity of this topic regarding the feasibility of their use. Will it be possible, in a future, to create an international databank of these kind of values? Could it be possible to compare these measured values between laboratories? Could these measured values be incompatible with human life applicable to all patients or should they be stratified by gender, age or ethnics? Are unlikelyhood limits as near as we can be of the values incompatible with human life?

Bibliography

1. Plebani M. The detection and prevention of errors in laboratory medicine. Ann Clin Biochem 2010; 47:101-10.
2. International Organization for Standardization. Medical laboratories — Quality managements systems—Requirements. ISO 9001. Geneva: ISO; 2008.
3. International Organization for Standardization. Medical laboratories — particular requirements for quality and competence. ISO 15189. Geneva: ISO; 2007.
4. Vogt W, Oesterle B. Extreme results in electrolyte determination [Article in German]. Wien Klin Wochenschr Suppl. 1992;192:21-7.
5. Arrive alive. <http://www.arrivealive.co.za/document/classification.pdf>
6. Cuhaci B, Lee J, Ahmed Z. Evaluating sodium bicarbonate controversy. Chest 2001;119:1622-3.
7. Macías Robles MD, López Fonticiella MP, Maciá Bobes C, Fernández San Martín A. Severe and acute hyponatremia in a schizophrenic patient with potomania. An Sist Sanit Navar 2009;32:117-20.
8. Kiekebusch H, Perucca E. Trombofilias hereditarias. Rev Chil Obstet Ginecol 2003;68:424-29.
9. International Union Of Pure And Applied Chemistry. Glossary of terms used in toxicokinetics (IUPAC Recommendations 2003). Pure Appl Chem 2004;76:1033–82.
10. Grocott MPW, Martin DS, Wilson MH, Mitchell K, Dhillon S, Mythen MG, Montgomery HE, Levett DZH. Caudwell Xtreme Everest expedition. High Alt Med Biol 2010;11:133-7.
11. Suárez-Vega I, Fuentes-Arderiu X. Reportable interval of patient examination results and ISO 15189. Clin Chem Lab Med 2005; 43:1278.
12. Solé-Enrech G, Fuentes-Arderiu X. Unlikeliness limits estimation. eJIFCC 2010; 21: <http://www.ifcc.org/PDF/publications/eJIFCC/vol21/03/eJIFCC_v21_03_05.pdf>
13. International Union of Pure and Applied Chemistry, International Federation of Clinical Chemistry. Properties and units in the clinical laboratory sciences-I. Syntax and semantic rules (Recommendations 1995). Pure Appl Chem 1995;67:1563-74.