DOWNLOAD PDF HORMONE ASSAYS AND THEIR CLINICAL APPLICATION

Chapter 1 : Hormone Assays and their Clinical Applications - Europe PMC Article - Europe PMC

The book deals with selected areas of hormone assays, but, reflecting the authors' own interest and expertise, the greatest emphasis is on reproductive endocrinology. Much of the clinical information in this area is based on the experience of the Endocrinology Unit at Edinburgh.

The existence of different meanings for this term when used in the present context is a source of confusion that has, among other things, led to erroneous ideas relating to immunoassay design. Such confusion should be terminated by adoption of one or the other of the definitions. However, the definitions are not of equal merit. Thus the many immunoassayists who now adopt the detection limit definition in accordance with the past recommendations of the IFCC 5 are neither unique nor revolutionary in this respect. Because this term is among a number for which formal definitions are currently being considered or reconsidered by NCCLS, this is a particularly opportune time to attempt to clarify its meaning and to resolve disagreements concerning its use that have persisted for 40 years or more. We therefore hope that a full debate on this topic will occur both among clinical chemists in this journal and elsewhere. Much semantic confusion in science stems from defining a term in a way that conflicts with its normal use. This has led to the recommendation by some authors that the word should be discarded from the scientific lexicon 6 7 8. Thus the starting point of any consideration of a scientific definition must be the generally accepted use of the word in the native language, albeit the formal definition may need to be more restricted or rigorous. Sensitivity, in turn, is generally defined as the quality or degree of being sensitive. More specifically, the OED defines the term as: Countless examples exist in the scientific literature of its use in this conventional sense. For example, Yi Qian et al. In these circumstances the second slope definition appears, as indicated above, to have been generally regarded as a logical consequence or corollary of the first. This assumption was explicitly enunciated by Yalow and Berson 10 in their section relating to immunoassay design. Sensitivity can be defined either as the minimal detectable concentration or the slope of the doseâ€”response standard curve. Then the minimal detectable quantity would be about 1 picogram. If the slope is fold greater, i. Thus assuming the experimental error is unchanged, increasing the sharpness of the doseâ€”response curve results in a reduction in minimal detectable quantity. It is instructive to analyze this superficially persuasive but, as advanced by Yalow and Berson in the course of a prolonged controversy relating to immunoassay theory see, e. It rests on two premises: Premise 1 is clearly open to doubt, and is, in practice, generally invalid. However, even if it can be shown to hold in a particular system, premise 2 must also be fulfilled. For example, if the measured response in a conventional RIA is the fraction of labeled antigen bound b and b is plotted against the analyte concentration [H] with linear coordinates as posited by Berson and Yalow in their analysis 10 , the slope of the curve for b vs [H] at zero dose will correlate inversely with the detection limit only if the standard deviation SD of bo i. For example, it is readily demonstrable that the maximal slope of the log b vs [H] curve â€”and hence minimization of the detection limit, assuming the CV of measurements of b remains constantâ€”is achieved as the antibody concentration and hence bo approaches 0. In contrast, the maximal slope of the b vs [H] curve is achieved when the antibody concentration is 0. However, use of this antibody concentration will minimize the detection limit only if the SD of bo remains constant. In short, the proposition 10 that increasing the slope of the b vs [H] curve implies reduction in the detection limit when the CV in bo is constant is specious. As indicated below, the assumption that the error in the response variable remains unaffected by changes in assay or instrument design is generally false. But the example also illustrates another important and related point, i. Thus, if sensitivity is identified with response curve slope, conflicting conclusions are likely to be reached regarding the conditions yielding maximal assay sensitivity, depending on the particular coordinate frame in which the response curve is drawn. Such absurdity is especially conspicuous in albeit not confined to the immunoassay field. As is well known, conventional RIAs rely on observation of the distribution of radiolabeled antigen between free and antibody-bound moieties, this distribution constituting the assay

response. Its determination invariably requires the experimental measurement of two quantities both of which are subject to random error: It is generally current practice to introduce a nominally constant amount of labeled antigen into the assay system, and to measure the signal emitted only by the bound or free fraction; nevertheless, the measurement of the total labeled antigenâ€"either by a pipette, or by countingâ€"is subject to error, and must be considered as a component of the assay response. Whichever of these fractions is experimentally determined, the labeled antigen distribution may be expressed in many different albeit equally legitimate ways: The dose variable may likewise be variously expressed, e. Response curves may, in turn, be plotted in terms of a combination of any of these dose and response variables. However, a change in assay design will generally produce differentâ€"often opposingâ€"effects on curve shapes, positions, and slopes. Clearly, it is nonsensical to suggest that the assay is simultaneously rendered more sensitive or less sensitive, or that its sensitivity is unchanged, as a consequence of the change in antibody concentration, depending on the way the response and dose variables are plotted. But absurdities of this kind inevitably follow from a reliance on the response curve slope per se as an indicator of assay sensitivity or, indeed, of any other aspect of assay performance. Such reliance nevertheless constitutes a conceptual trap into which many immunoassay practitioners and theoreticians have fallen, and underlies much of the mythology that exists in this field. Referring again to an example drawn from a recent issue of Clinical Chemistry 18 , construction of an immunoassay is described essentially on the basis of the slope definition of sensitivity. The authors claim to have selected monoclonal antibodies for use in a competitive enzyme immunoassay on the basis of three criteria: However, the term sensitivity appears in several articles in this and other recent issues of Clinical Chemistry, where its meaning is indeterminate. Though immunoassay represents an analytical technique that because of the variety of ways legitimately used to plot doseâ€"response curves exposes the contradictions stemming from the slope definition, many other analytical methods and instruments can be shown, on examination, to illustrate the same point. For example, the response of a simple balance can be portrayed either as the distance moved by the pointer tip, or the movement of the balance beam, or the angle through which the pointer rotates, when a weight is placed on the pan. This example illustrates another albeit related problem associated with the slope definition. For these reasons, Mettler, the well-known balance manufacturer, strongly criticized the slope definition adopted by the American Chemical Society 19 on the grounds of its unworkability and abandoned the use of the term sensitivity in its own descriptive literature. Likewise, Jones, writing in in a radio engineering journal 3 , recommended that, for much the same reasons, this term should be discarded from the scientific vocabulary. A further criticism of the slope definition is that it precludes comparison of the sensitivities of two analytical methods or instruments such as ultraviolet and immunoassay methods to determine steroid hormone concentrations that rely on different response variables. The slope definition precludes reference to this feature as sensitivity. This quotient possesses the physical dimensions of the dose or stimulus, and represents the statistical error in the dose measurement, i. This quantity is independent of the manner in which the response curve is plotted; thus the same conclusion will be reached in regard to which of two immunoassay methods yields the more precise measurement of a specified analyte concentration irrespective of the coordinate frame used to plot the doseâ€"response curve. Clearly, the precision of measurement of any defined baseline amount or concentration determines the smallest difference or change in amount to which the measurement system yields a perceptible i. In particular, the resolving power of many analytical systems including RIAs , a quantity implicitly determined by the standard deviation of the selected baseline analyte concentration, varies with concentration see Fig. Moreover, this definition conflicts with the basic meaning of sensitivity i. For this reason, we and our past coworkers have, in our theoretical studies relating to ligand assay design and optimization e. On the other hand, an analyst for whom it is important to distinguish between samples that contain and those that do not contain a specific analyte e. This depends on the number of replicates used, the confidence demanded, etc. In other words, the detection limit as thus determined depends both on the performance characteristics of the measuring system itself i. In reality, this quantity simply constitutes what Spencer evidently though doubtless with good reason regards as the

effective lower limit of the working range of thyrotropin assays used in clinical practiceâ€”the working range being defined as the range of concentrations or amounts over which measurements are of a precision acceptable to the analyst see 8 17 ; Fig. Spencer and her colleagues are, of course, free to decide when thyrotropin measurements are of acceptable precision in the particular context in which they use such assays; however, the needs of other investigators may be more or less stringent than hers, and their definitions of the working range of particular thyrotropin assay systems will vary accordingly. Moreover, an analyst concerned with, e. In short, the working range of an assay is defined by numerical limits that are a matter of local choice; these limits should not, therefore, be incorporated into a formal definition. A second objection to the use of the term functional sensitivity is that it introduces yet further semantic confusion into an area that is already widely misunderstood and controversial. As correctly emphasized by Sadler et al. Our own view is that the performance characteristics of an immunoassay kit or method can be best represented by its precision profile 8 25 , an approach being adopted by many immunodiagnostics companies and investigators e. Assay biasâ€”in so far as this is a valid conceptâ€”is potentially the subject of another debate and is not addressed here. It is likewise applicable in principle to all other analytical techniques. Though certain secondary assay parameters e. Whether or not it is useful to devise additional nomenclature that identifies, e. Clearly, such terminology must be carefully chosen to avoid conceptual ambiguity. In summary, we have here attempted to demonstrate that the response curve slope definition of sensitivity is untenable, that it leads to many absurdities and confusion, and that its retention would effectively exclude the term from the scientific lexicon, leading as has been claimed to be a consequence of the formal identification of accuracy with absence of bias 6 to a depletion of linguistic resources. In other words, no English term would be available to describe an instrument or method capable of measuring small quantities of that which it is designed to measure, nor would any adjective exist describing a method capable of determining smaller amounts than another. It is therefore incumbent on the protagonists of the slope definition to justify its utility and, most particularly, to indicate if they regard an improvement in sensitivity as thus defined as advantageousâ€”and, if so, on what grounds. Open in new tab Figure 1. Theoretical immunoassay doseâ€”response curves relating to a range of antibody concentrations plotted in terms of: Concentrations are expressed as multiples of the reciprocal of the equilibrium constant K , assumed to be identical for label and analyte. The labeled analyte concentration is assumed to equal 0. Open in new tab Figure 2. Open in new tab Figure 3. The statistical error may be that observed within an assay batch, between batches, between laboratories, and so forth. The working range may be defined as the range over which assay results are of acceptable precision to the analyst, and clearly depends on the particular context in which the assay system is being used. Brochure discussing inapplicability of American Chemical Society definition of the sensitivity of a balance circa Phenomenological description of the response and detecting ability of radiation detectors. Proc Inst Radio Engineers ;

Chapter 2 : Hormone Assays and Their Clinical Application | JAMA | JAMA Network

This second edition bears little resemblance to the first (), for the field of endocrine assays has experienced a phenomenal growth in the past ten years.

Chapter 3 : Point On the meaning of â€œsensitivityâ€• | Clinical Chemistry

Full text Full text is available as a scanned copy of the original print version. Get a printable copy (PDF file) of the complete article (K), or click on a page image below to browse page by page.

Chapter 4 : Hormone assays and their clinical application.

Hormone Assays and Their Clinical Application [John Alexander Loraine, Edwin Trevor Bell] on

DOWNLOAD PDF HORMONE ASSAYS AND THEIR CLINICAL APPLICATION

*calendrierdelascience.com *FREE* shipping on qualifying offers. Book by Loraine, John Alexander, Bell, Edwin Trevor.*

Chapter 5 : Hormone Assays and their Clinical Application - Europe PMC Article - Europe PMC

*Hormone Assays and Their Clinical Application [John Alexander Loraine, Edwin Trevor Bell] on calendrierdelascience.com *FREE* shipping on qualifying offers.*