Ten years' experience with an external quality control program for semen analysis

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Objective: To gauge the performance of laboratories and impact of the German semen analysis external quality control program (QuaDeGA) over its first 10 years.
Design: Retrospective analysis of QuaDeGA's twice yearly distribution of fixed semen samples and electronic material documenting sperm motility. Ranking of each participant's responses was determined according to their relation to a "target window."
Setting: Multicenter.
Paitent(s): Healthy donors.
Intervention(s): None.
Main Outcome Measure(s): Laboratory performance, World Health Organization (WHO) adherence.
Result(s): Over 19 runs, there was a steady increase of participants (280 laboratories), the largest group being private urologic practices. Although use of WHO-recommended Neubauer chamber (from 33% to 55%) and diluent (from 11% to 32%) increased, the opposite occurred with morphology staining protocols (from 41% to 19%). Overall, <8% of laboratories truly followed WHO guidelines. Median-based comparisons, replacing reference laboratories, resulted in a merging of performance rankings regardless of the protocols used.
Conclusion(s): Adherence to WHO recommendations is low, with the majority of laboratories using methods expressly opposed by the guidelines. Participation in QuaDeGA was found to improve the performance of the laboratories involved in the program. However, the use of median-based ranking, while decreasing the extent of variance between laboratories, brings into question the significance of the rankings. (Fertil Steril® 2012;98: 611–6. ©2012 by American Society for Reproductive Medicine.)
Key Words: Quality assurance, semen analysis, multicenter, WHO

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Despite the development of many sophisticated analytic techniques, the long-established "traditional" procedures for the examination of semen (i.e., volume, sperm count, motility, viability, morphology, etc.), remain the main tools for the clinician and researcher investigating male fertility. On first impression, routine semen analysis appears to be straightforward, because it comprises a series of macroscopic and microscopic assessments that are easily performed in a suitably equipped laboratory by competent staff. This view, however, discounts numerous pitfalls that are potential sources of inaccuracies and imprecision. For example, the veracity of sperm number/concentration assessments can be undermined by sampling errors caused by the nature and constituents of semen, and motility and morphology evaluations depend on the training and specialist knowledge of those performing these subjective appraisals.

The need for standardization of these procedures was the impetus for the publication by the World Health Organization (WHO) of their laboratory manual in 1980 (1). Recently released in its fifth edition (2), the manual offers detailed advice on every aspect of semen analysis and as a consequence has become the criterion standard for the field. Its impact has been such that "performed according to the WHO guidelines" has become a ubiquitous

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expression in publications and presentations dealing with research, diagnosis, or treatment of male infertility.

The importance of quality control for the maintenance of the accuracy, precision and competence of laboratories as well as the detection and correction of possible errors was first highlighted in the fourth edition of the manual (3). The significance of quality control was further emphasized in the fifth edition (2), where the chapter was expanded. The need for consistency in the performance of semen analyses was also the stimulus for the German Society of Andrology (DGA) to establish an external quality control (EQC) program: QuaDeGA (Qualitätskontrolle der Deutschen Gesellschaft für Andrologie; www.quadega.de). Following in the footsteps of already established programs in the United Kingdom (UKNEQAS) and that of the European Society of Human Reproduction and Embryology (ESHRE), QuaDeGA started as a voluntary service for members of the DGA, but soon incorporated and has been increasingly used by nonmembers. The German Federal Medical Board (Bundesärztekammer) has worked on the inclusion of andrology laboratories in their "Guidelines on Quality Assurance of Medical Laboratory Investigations" (Rilibäk [Richtlinien der Bundesärztekammer]). Beginning in January 2011, participation in a quality control program has become compulsory in Germany for all laboratories performing semen analysis (with a transition period of 2 years) (4). In preparation for the inclusion of QuaDeGA into Rilibäk, the manner in which the target range was calculated was changed in 2008 (run 13) to comply with the Bundesärztekammer's requirements.

Because the first 10 years of QuaDeGA have coincided with the tenure of the recently superseded WHO manual, our aim was to gauge the impact of QuaDeGA on the performance of laboratories and assess the compliance of the participants to the former 1999 WHO recommendations.

MATERIALS AND METHODS

Samples and Distribution

The collection and use of the semen samples distributed in the QuaDeGA program was approved by the Ethics Committee of the University Hospital Muenster and the State Medical Board. Written informed consent was obtained from different healthy donors who provided samples after 2–5 days' sexual abstinence. The ejaculates were mixed to provide two lots (one high and one low sperm concentration), sperm motility (one good, one poor) in each lot was recorded in a minimum of five different microscopic fields (×400 magnification) per sample with the use of standard video equipment, and the remaining semen was then fixed for morphology assessment. Initially a 4% (vol./vol.) formalin solution was used, but this was replaced in the eighth run by sodium azide (3 mmol/L) to avoid occasional fixative-induced sperm agglutination.

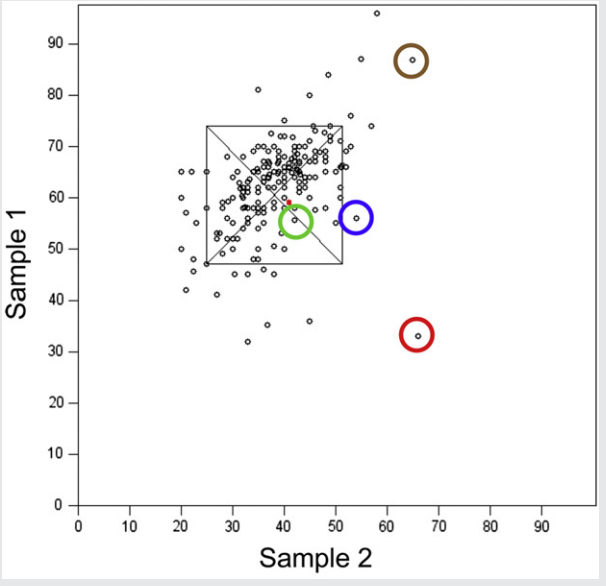
Twice yearly, each laboratory participating in QuaDeGA receives two tubes containing 0.5 mL fixed semen for the determination of concentration and percentage normal morphology. The choice of methods used for these assessments are at the discretion of each laboratory to reflect the methods routinely used; however, the samples are accompanied by a leaflet detailing the WHO recommendations for microscopic optics, counting chamber, diluent solution, and staining methods. No justification or comparison of the procedures used was required or requested. In the participating laboratories, the analyses were performed by certified technicians under the supervision of physicians or scientists.

For the first 17 QuaDeGA runs, optical discs (CD or DVD) containing recordings of ten different microscopic fields per sample were distributed for the determination of sperm motility. From the 18th run onward, the motility recordings were placed onto the program's website (www.quadega.de) as a video embedded into an open source (GPL 3) video player. For both types of video access, participants were instructed to assess sperm motility (duplicates of 200 sperm for each sample) and provide a mean for each motility grade. For the first 18 runs, motility classification was assessed using the four-tier system recommended in the fourth edition of the WHO manual (3). This changed in the 19th distribution to the three-step grading system recommended in the new manual (2). Because of this alteration, motility assessments from run 19 were not included in any comparisons.

QC Assessment

To assess the degree of agreement of the results and thence the performance of each participating laboratory, a Youden plot (Fig. 1) was constructed at the end of each QuaDeGA run, and the results from each participant were ranked according to their relation to a "target window." Rank 1 was awarded when values from both samples were within the target window, rank 2 when one value was outside, rank 3 when both were either above or below the desired range (i.e., a systematic

FIGURE 1



A Youden plot constructed from progressive motility results obtained from laboratories participating in the 19th run of QuaDeGA. The median reference range is indicated by the box, and the colored circles show examples of the various rankings: rank 1 (*green*), rank 2 (*blue*), rank 3 (*brown*), and rank 4 (*red*).

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