



Educational Discussion: Human Chorionic Gonadotropin (hCG)

2017-C Chemistry (C)

Practices and Recommendations for Reporting Quantitative Human Chorionic Gonadotropin (hCG) Test Results

The General Chemistry (C-B 2017) Survey included supplemental questions to determine the different hCG reference intervals that clinical laboratories use to report results of quantitative hCG tests and to determine the hCG cutoffs that may be used to assign interpretive comments. Other questions asked about the use of hCG tests in specific populations and their associated reference intervals. Complete or partial responses were received from 3,568 laboratories.

Tests for hCG are commonly used to determine a woman's pregnancy status. Both qualitative and quantitative hCG tests are available for this purpose but the results are not interpreted similarly. Qualitative test results are binary (ie, negative or positive) and so interpretation of the test result is unambiguous. In contrast, quantitative test results are discrete and interpretation is usually accomplished by comparison of the numerical result to a reference interval.

hCG Reference Intervals in Females

Only 30% of laboratories provided a single reference interval or cutoff when reporting quantitative hCG test results in females. Figure 1 shows that 5 IU/L is the most frequently used upper reference limit (70%). Of note, a reference interval of less than 5 IU/L for non-pregnant women has been validated by Snyder, et al¹. A cutoff of 25 IU/L was used by 15% of laboratories with other cutoffs used less frequently.

42% of laboratories provide an interpretation of quantitative hCG results (ie, negative, positive, and/or indeterminate for pregnancy) based on different hCG cutoffs or intervals. Of these, 32% reported negative and positive interpretations, 29% reported only negative interpretations, 22% reported negative, indeterminate, and positive interpretations, and 14% reported only positive interpretations. Other combinations were reported by the remaining 3%. Laboratories that do not include an indeterminate interpretation most frequently use a cutoff of 5 IU/L to discriminate between results reported as negative or positive. In contrast, laboratories that report all three interpretations most frequently use a cutoff of 5 IU/L to identify negative results, 25 IU/L to identify positive results, and interpret results as indeterminate if the value is between 5 and 25 IU/L (Figure 2).

hCG Reference Intervals by Gestational Age

Maternal serum concentrations of hCG change throughout pregnancy. The concentration increases rapidly during the first trimester reaching its peak at 8 to 10 weeks of gestation after which it declines by approximately 90% of the peak by the end of the second trimester. Gestational age-specific hCG reference intervals have been reported but tend to be very wide which limits their clinical usefulness. Despite this, 59% of respondents reporting using gestational age-based reference intervals when reporting hCG results in females.

hCG Reference Intervals by Chronological Age

Studies have suggested that age-based hCG reference intervals would be clinically useful given the not uncommon clinical practice of measuring hCG without regard to a woman's age or reproductive history.^{1,2} Only 9% of responding laboratories indicated the use of age-based hCG reference intervals.

hCG Reference Intervals in Males and in Oncology Applications

hCG testing can be indicated in males as it has clinical utility as a marker for testicular germ cell tumor. Only 25% of responding laboratories reported providing male-specific hCG reference intervals. Of these, 95% used a cutoff value of 6 IU/L or less with the most frequently used cutoff being the same one most often used for females (5 IU/L) (Figure 3). 62% used a cutoff that was lower than 5 IU/L. A male-specific hCG reference limit of less than 2 IU/L has been reported³ but only 18% of laboratories used this limit.

Similarly, hCG testing in serum and/or cerebrospinal (CSF) fluid is used as a tumor marker in other malignant disorders (ie, gestational trophoblastic disease, intracranial germ cell tumor). Only 13% of responding laboratories indicated that they offered a separate, orderable test for hCG as a tumor marker, nearly all (99%) of which offered it only in serum or plasma and not in CSF. 95% used a cutoff value of 10 IU/L or less with 5 IU/L being the most frequent used cutoff (Figure 4).

Sources of hCG Reference Intervals

The most frequently cited source for the hCG reference intervals used by responding laboratories was the manufacturer’s product insert (56%) followed by scientific literature (10%) and internal laboratory studies (6%). 29% of laboratories were not certain of the source of the hCG reference intervals that they used.

References

1. Snyder JA, Haymond S, Parvin CA, Gronowski AM, Grenache DG. Diagnostic considerations in the measurement of human chorionic gonadotropin in aging women. *Clin Chem.* 2005;51(10):1830-1835.
2. Patel KK, Qavi AJ, Hock KG, Gronowski AM. Establishing reference intervals for hCG in postmenopausal women. *Clin Biochem.* 2017;50(4-5):234-237.
3. Greene DN, Petrie MS, Pyle AL, et al. Performance characteristics of the Beckman Coulter total β hCG (5th IS) assay. *Clin Chim Acta.* 2015;439:61-67.

Figure 1. Upper limit of hCG reference interval used for females

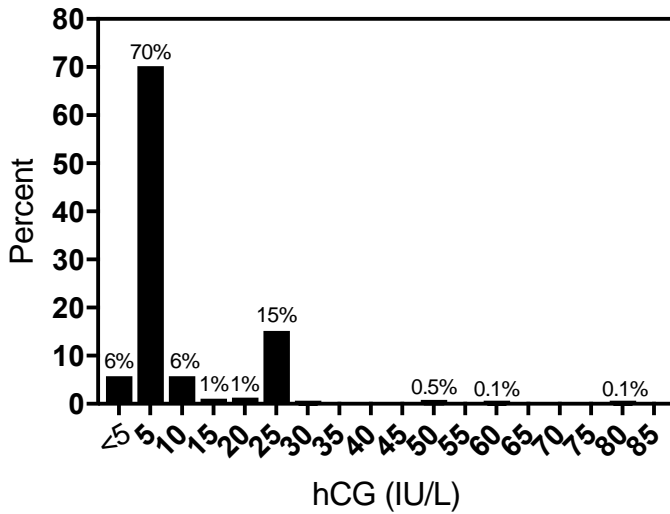


Figure 2. hCG cutoffs used by laboratories when results are reported with an interpretation of “negative,” “indeterminate,” or “positive” for pregnancy

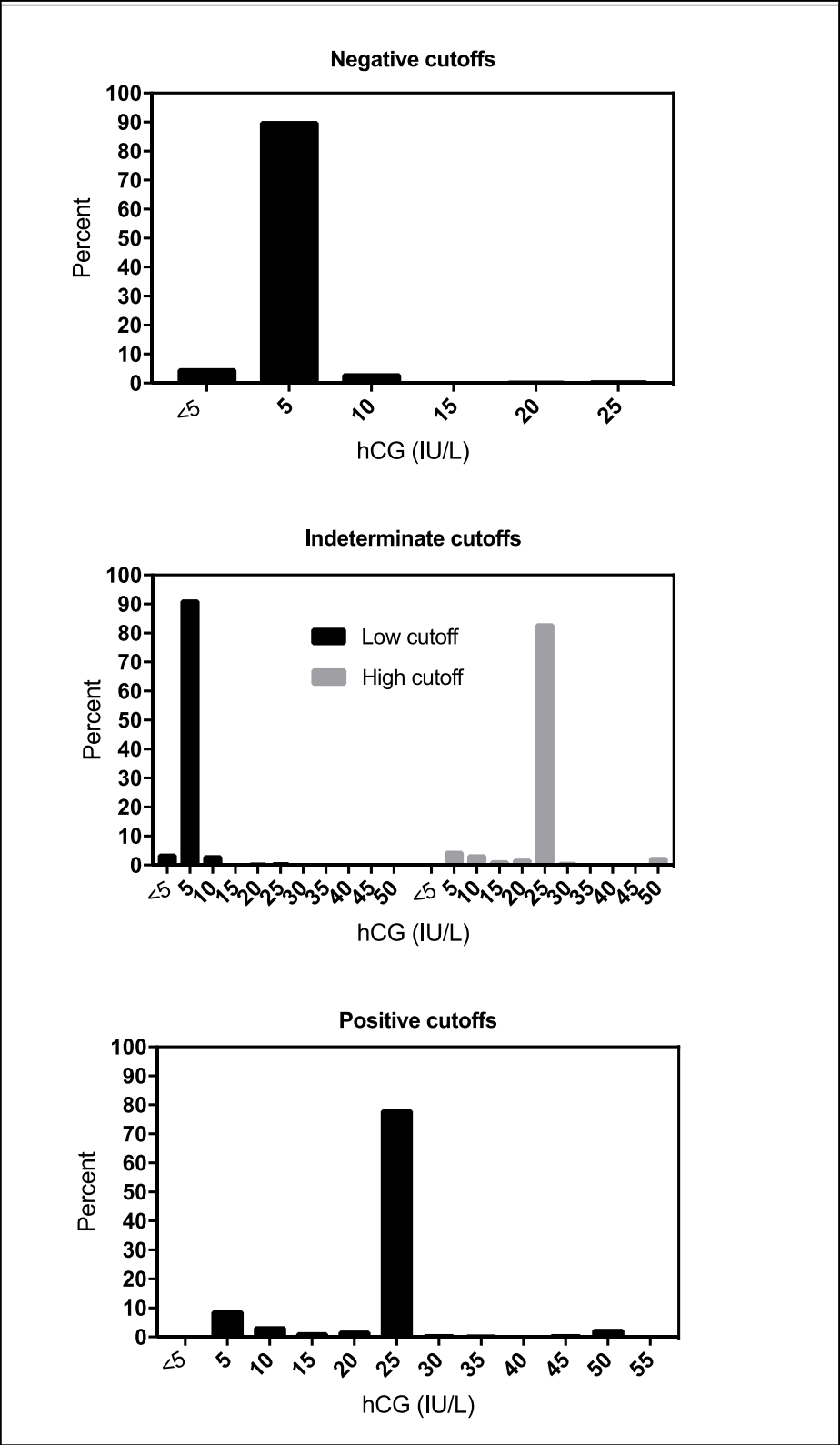


Figure 3. Upper limit of hCG reference interval used for males

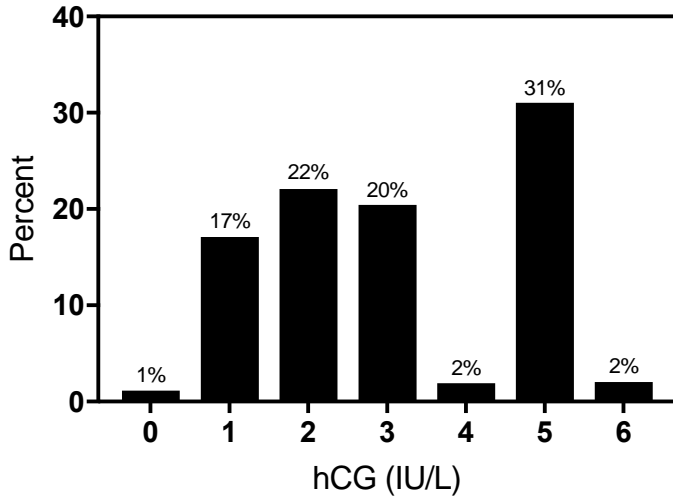
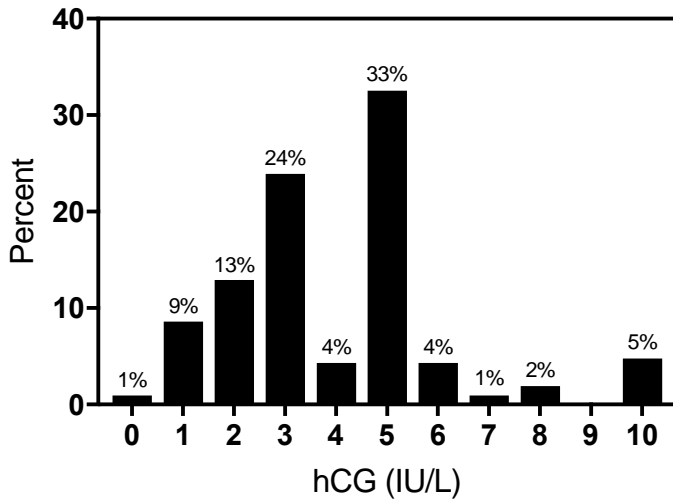


Figure 4. Upper limit of hCG reference interval used for oncology applications



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