Clinical Chemistry Trainee Council
Pearls of Laboratory Medicine
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TITLE: Point-of-Care Testing

PRESENTER: Dina N. Greene, Ph.D, DABCC

Slide 1:
I'm Dina Greene and this lecture will provide a brief introduction to Point-of-Care (POC) testing, which is testing that can be performed at the site of patient care.

Slide 2:
The take home points from this lecture will include an introduction to why and where we use POC testing, the plusses and minuses of this laboratory branch, and the different types of measurements, more specifically quantitative versus qualitative.

Slide 3:
By definition, POC tests are those that can be performed close to the site of patient care. This can be in a primary health care office, in a hospital, as self monitoring, at a health fair, or in a third world country. POC tests are designed to either give a plus or minus qualitative result, or in other cases, a precise numerical measurement. Depending on the testing, the College of American Pathologists (CAP) will deem these tests either waived or moderately complex. Waived tests will not require laboratory personnel to perform the tests, and regulatory guidelines are minimal because the risk posed to the patient by an erroneous result is considered minimal. Other POC tests are labeled as moderately complex, and will therefore require more training, competency, and quality measures. Although both waived and moderately complex tests require validation and training, it is important to know which CAP guidelines are necessary to follow for a particular device. Since the CAP is specific to the United States, if you are watching this from an alternative location, it is important to be aware of the specific regulatory parameters adopted by the government agencies specific to your country.

Slide 4:
Validation of POC instruments is a critical component of a successful POC implementation. The most important components of a validation are precision, accuracy, and method comparison. The method comparison component is extremely valuable; physicians and the laboratory must be able to identify how/if the POC results will differ from the results derived from the automated instrumentation in the central laboratory. In addition, quality control should be run regularly to maintain competency in the staff and to assure that the devices are performing accurately. Timing intervals for QC will vary

based on assay and volume. It is also noteworthy to be reminded: the results of the POC tests are highly dependent on the person performing and analyzing the results. This can add additional bias to the results that may not have been observed in the analytical validation.

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As with anything in laboratory medicine, there are general advantages and disadvantages to POC testing. Here I have listed some of the most noteworthy advantages. In theory, POC testing should have a faster turn around time, since no specimen transport is required, and the test is performed bedside. The second advantage has to do with specimen requirements; many POC tests use <300 microliters of capillary blood or urine. In addition, no processing is required for urine or whole blood. Finally, and arguably the most important advantage of POC testing is that they provide an avenue to align laboratory testing with clinical patient flow.

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And now onto the disadvantages. In general, POC testing will come at an increased cost, as each specimen often requires its own individually packaged device or testing strip. Quality is a concern because often times, nurses or other non-laboratory personnel will be performing the testing. These persons have many other responsibilities aside from laboratory testing, which can lead to distractions during testing or other quality facets overlooked. For example, capillary samples are often used for certain POC tests, such as hemoglobin. Depending on the skills of the person collecting the capillary sample, the imprecision of the measurement can vary greatly. In addition, even if performed correctly, some POC devices may not be as precise, accurate, and/or as analytically sensitive as their automated laboratory counterparts. Compliance is a huge concern with POC tests, as documentation of results, users, and competency can be very difficult when there are a variety of personnel performing the testing. Billing is also problematic with POC testing. In order to bill for a lab test, the test must be ordered by a physician. For many POC tests, like glucose, it is standard of care to quantify the result. This makes it increasingly difficult to receive a physician order for every glycemic status tested. Finally, all of these POC disadvantages require a strong link between the clinical staff and IT. Since IT is generally not familiar with the lab, and the clinical staff is generally naïve to IT, they must work together to create a process for the POC testing that limits these disadvantages.

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I have outlined here a few of the clinical favorites in POC testing. For qualitative tests, using human chorionic gonadotropin (hCG) as a marker for pregnancy is one of the oldest and most widely used POC tests. Others include detecting infections, like the rapid strep test, screening for drugs of abuse and the flu, and general urinalysis chemistries. For quantitative testing, glucometers are the most utilized in the clinic, but blood gasses, electrolytes, creatinine, HbA1c, C-reactive protein (CRP), D-dimer, and troponin are also becoming increasingly common. It is important to note that there is much debate on the adequacy of the sensitivity and the specificity of the troponin POC tests, which makes a valuable point: just because a POC test is commercially available doesn't mean that it meets the clinical needs of your patient population.

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To provide more exposure into the chemistry behind POC testing, I will review three short cases. The first two use qualitative POC tests, while the last uses quantitative.

Slide 9:
In our first case, "Am I pregnant?", a teenager presents to a clinic worried of pregnancy. She had unprotected sex a few days earlier. Urine was collected for a POC pregnancy test.

Slide 10:
POC pregnancy tests work by immunodetection of hCG. There is a well for the specimen to be applied, which contains lyophilized antibodies. Then there is a separate window where the solid phase antibodies are embedded and the result can be read.

Slide 11:
This animation shows the mechanism of hCG detection using a generic POC device. Here you add your specimen to the well. The specimen solubilizes the detection antibody matrix, and the fluid travels via capillary action through the device. In this specimen, hCG was present, represented by the blue proteins, so two lines would be visualized, one line as a control for proper wicking and motility, and a second line denoting hCG is present.

Slide 12:
In the specimen collected from the teen, the POC test was negative. Can we rule out pregnancy? No. POC hCG assays are not designed to rule out early pregnancy. Their analytical sensitivity is not low enough to often detect the trace amounts of hCG present early in conception. Following-up with a quantitative serum hCG or retesting with a POC device in a few weeks can more definitively rule out pregnancy.

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Our next case looks at screening for drugs of abuse using POC devices. Here we have an outpatient that has enrolled themselves in rehab for drug addiction. They meet with their counselor 2x/week for psychological support. During this time, it is important for the counselor to know if the patient has relapsed, as the therapy session can be differentially focused depending on recent abuse.

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Like hCG POC testing, drugs of abuse are most often detected using an immunoassay. However, in contrast, these assays are typically competitive. In a competitive assay, you have lypholized labeled drug – shown here as pink lightening bulbs - and control antibodies. Impregnated in the membrane are the solid phase antibodies, specific to multiple drug classes. When urine is added to the cup, the lypholized labeled drug and control antibodies will be dissolved and can migrate via capillary action through the membrane. Either drug in the patient specimen, or labeled drug from the device will bind

to their specific solid phase antibody. In this case, there was no drug in the specimen, so a band will form at the specific drugs site.

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Here we have a case that there is drug present in the urine. The unlabeled drug will be in a molar excess to the labeled drug, and will therefore saturate all of the solid phase antibody. No band will form.

Slide 16:
These are the results from our patient of interest. The first thing to notice is the control band. This shows that the volume of urine was sufficient and proper for wicking and migration to occur. For the results of the drug screen, we can see three places where there is no line present, implying drug use. Following these places where there is no line present up to the drugs key above points to methamphetamine, amphetamine, and propoxyphene in the urine.

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For definitive detection of drugs in the specimen, a confirmation assay such as mass spectrometry should be utilized. Since both false positive and false negative results may be seen, these tests should not be used as background for sanctions such as exclusion from school, job dismissal, or loss of parental rights. However, since this screen was for counseling purposes, these results can be used for the therapist to guide her counseling.

Slide 18:
For our last case, we will take a quick look at POC glucometers. Here we have a 76-year-old man who is having his glucose checked. He is non-fasting and the POC device reports out that his blood glucose is >400 mg/dL. The nurse was skeptical of this result, so she sent another sample to the lab. The lab results showed that he was normoglycemic. Which is correct?

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The POC device that was used to measure the man's glucose quantifies the analyte using an enzymatic reaction. Glucose dehydrogenase will oxidize glucose to D-glucono-delta-lactone. This reaction requires PQQ as a cofactor, which accepts the electrons from the oxidation reaction. The transfer of electrons creates a current that can be measured by the glucometer. The current generated will be directly proportional to the amount of glucose in the specimen.

Slide 20:
The automated assay used to quantify glucose was also enzymatic, but used a coupled reaction of hexokinase and G6PD to oxidize glucose, in turn reducing NAD+ to NADH, which can subsequently be measured as a change in absorbance overtime. The rate of change of the absorbance is directly proportional to the concentration of glucose in the specimen.

Slide 21:

The GDH-PQQ method is prone to interference by non-glucose sugars. This interference has resulted in multiple deaths. Death occurs when the patient is treated for the apparent hyperglycemia, but then becomes critically hypoglycemic. The FDA has issued multiple warnings to address this problem. In this case, the patient was receiving a nutritional supplement that contained fibersol, which is a modified maltodextrin. Since maltodextrin is a sugar polymer, this scenario parallels the incidences addressed by the FDA.

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In conclusion, POC testing can provide rapid results in the clinical flow. Although this is seemingly quite attractive, and can be beneficial to patient care, POC testing is not as simple as it appears.