HAMILTON REGIONAL LABORATORY MEDICINE PROGRAM

LAB CONNECTIONS

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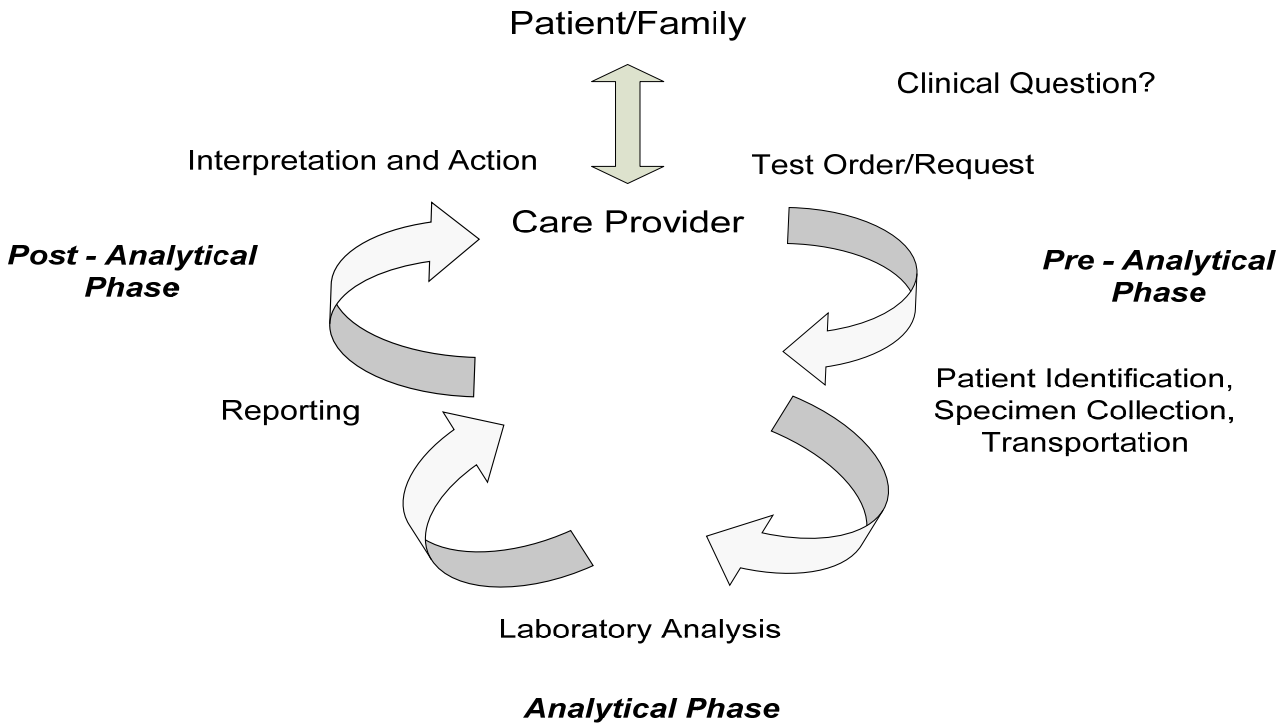
The HRLMP offers over 1500 tests on our menu and produces over 10 million test results each year. Our quality goal is to provide accurate, reproducible and clinically relevant test results. To do this, we have in place a Quality Management System that provides direction to our 650 technical, medical and scientific staff regarding all pre-analytical, analytical and post-analytical activities. Some of these are highlighted in this issue.

The best test, the right patient, the correct result - Laboratory testing for effective patient care

The total test process



As seen in this diagram, the testing process begins with the request from the care provider, who has a question about his/her patient's condition and involves many steps before a result is reported and acted upon. Errors can be made in any of the steps and for the patient/family it does not matter where in the testing process the error occurs. The important thing is, that they are caught before it can do harm. In this issue we point out some of the features of our Quality Management System that prevent errors.

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The Test Request: (Quality goal - the best test for the clinical question)

The choice of the appropriate test for the diagnostic question is important for effective and efficient patient care and should be a marker for laboratory quality. Inappropriate test selection is difficult to quantify but the laboratory should be more involved in guiding test selection.

Choosing the Correct test - A Geneticist's viewpoint

In Molecular Diagnostic Genetics, the indications for many tests are complex and often involve careful assessment of other laboratory test results for the index case as well as other family members. For hemoglobinopathy investigations, it has been our experience that a significant proportion of all cases have been referred for the molecular tests that do not adequately address the clinical phenotype or family history. The most common scenarios we encounter are vague or ambiguous requests for *hemoglobinopathy testing* or *thalassemia testing*, or requests for the incorrect tests (*e.g., β-thalassemia* rather than *α-thalassemia*). To ensure that the correct test(s) has been ordered and to minimize the volume of unnecessary tests, all referrals for hemoglobinopathy investigations are required to provide the most recent hematology results (CBC, hemoglobin analysis). Each case begins with an assessment of the clinical indications and family history to determine the most appropriate panel of tests. In many cases, this results in a different test being ordered or additional tests being added to the original request. Upon completion of the molecular genetic tests, the case is reassessed to determine if further testing is indicated.

Test Utilization initiatives at the HRLMP

Recently the HRLMP introduced several initiatives to guide use of certain tests. These were done using best practice and evidence-based approaches and are described below:

- Tests were identified for utilization quality review

This was initiated by laboratory physicians or scientists who have an interest in specialized areas of clinical medicine. For example, a clinical hematologist identified overuse of APTT in the hospitals (1).

- Laboratory data review

Once the test has been identified, a review of the test utilization is made through an inquiry to the laboratory information system. For example, we looked at the red blood cell folate results over a period of one year and observed that there were no results indicating a deficient red blood cell folate perhaps due to fortification of foods (2). The number of tests performed and the cost of the assay made this an expensive test that provided no useful clinical information.

- Review of evidence

Following confirmation that the identified test may no longer be warranted and its de-listing would enable significant savings, a review of the literature is undertaken to establish the clinical utility including clinical guidelines indicating that the test is required. This enables us to adequately inform users as to why the test is no longer required. If we find the test has some utility, we need to make provision for this. For example, we reviewed the literature for the use of serum amylase in the context of acute pancreatitis. It is quite clear that serum lipase is a better diagnostic test (3). However, the use of serum amylase for selected other gastrointestinal conditions may still be required.

- Matching laboratory practice to guidelines

Other changes have been made to conform to national and international guidelines. For example, the restriction on HbA1c testing to once every 3 months is in keeping with the 2008 Canadian Diabetic Association guidelines.

As the HRLMP strives to measure all aspects of Laboratory Quality we will need to develop robust tools to identify evidence-based test ordering practice and tools to monitor how our requesting physicians comply with best practice. As a practical example, the laboratory is actively and collaboratively engaged in the development and delivery of appropriate evidence-based laboratory “order sets”.

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The pre-analytical steps: (quality goal – the appropriate sample from the right patient)

Once the test is ordered, the proper technique for both the collection and labeling of laboratory specimens need to be followed (4). Acceptance of the sample by the laboratory is based on defined requirements for collection and correct patient identification. In addition to the laboratory information guide (5), there are a number of initiatives for reducing errors. For example, the microbiology laboratory has been involved in initiatives to improve specimen quality.

The first of these was the "*Swabs Don't Do the Job*" campaign in 2005. The laboratory reached out to clinical areas with educational posters, emails and in-services to relay the message that swabs are less sensitive than tissues or body fluids for the detection of microorganisms. This campaign improved communication between the clinical areas and the microbiology laboratory and reduced the number of swabs sent for culture from sterile sites.

In 2007/08 the microbiology laboratory was engaged in the "*Clean care is safe care – Be a Star*" education program to ensure that proper aseptic technique is used in collecting blood cultures. This is important for patient safety as it prevents blood culture contamination and the unnecessary use of antibiotics. Blood culture contamination rates were reduced for at least 3 months following the program.

In 2009 the laboratory responded to high specimen rejection rates with the "Microbiology Specimen Container Guide" (5). This is a visual guide of the correct containers to use for different types of microbiology specimens. The guide has decreased the number of stool and viral culture rejected specimens, but did not impact specimen rejection rates overall.

These initiatives were all followed by improvements in specimen quality. The findings have been shared with healthcare providers at the annual Hamilton Health Sciences Patient Safety Symposia to demonstrate how high quality specimens improve patient care.

The laboratory analysis: (quality goal - accurate, reproducible and clinically relevant test results)

Clinically relevant test

The evaluation of any new test begins with an understanding of the clinical need. Several questions are asked:

1. Will the test be used for screening or monitoring treatment?
2. Does the new test provide improved diagnostic capability?
3. What performance characteristics are most important to satisfy the clinical need?

These questions are asked when we change the method for an existing test on our menu or bring in a new instrument. The new test or instrument must then be validated before it is made available to our users. A rigorous validation is undertaken to assess each test method's performance characteristics for accuracy, reproducibility, sensitivity and specificity.

Selecting the appropriate assay to meet the diagnostic need - the G6PD story

G6PD deficiency, the most common hereditary enzyme defect, is estimated to affect 400 million people worldwide. Most patients are asymptomatic although this deficiency may manifest in acute or chronic hemolytic anemia or be associated with severe neonatal hyperbilirubinemia. Therefore, the Canadian Pediatric Society and American Academy of Pediatrics have recommended screening for G6PD deficiency in neonates presenting with hyperbilirubinemia. The current G6PD screening test and assay was developed for detection of marked deficiency in an adult population and have well known limitations for different patient groups. In neonates, the normal reference values of G6PD enzyme activity are much higher than adults and may not be detected using the current screening and assay methods. Also, since this disorder has a sex linked inheritance, heterozygous females may have assay values that fall within normal reference intervals,

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specifically if samples are collected during acute hemolysis, when G6PD enzyme activity is known to be higher. In response to the new pediatric recommendations, the HRLMP Molecular Hematology and Genetics Laboratory have developed molecular diagnostic techniques to detect G6PD deficiency in the neonatal and heterozygote female patient groups. Much work has been done to perform genetic sequencing of all samples referred for G6PD screening for identification of the most common mutations found in Ontario's multi-ethnic population. As a result, molecular screening for G6PD deficiency is now available through HRLMP using a combined strategy of Polymerase Chain Reaction (PCR) and DNA sequencing to positively identify all patients with suspected G6PD deficiency.

Maintaining test performance

Once a test is introduced into the laboratory, we have many ways of monitoring and maintaining our performance of these tests. Our laboratory staff are trained and qualified for the work they do. Staff must be trained on each new test method and the operation and maintenance of the equipment. Competency is assessed as part of this training process.

All patient test results are performed in conjunction with quality control samples with known target values that must meet certain criteria before the patient test results are released. Our quality control program is designed to detect any errors occurring during the testing process. It also provides us with the ability to monitor the performance of the test over time.

The laboratory participates in external quality assessment programs for all tests. Some are formal programs which provide samples for testing where the test result is unknown. We submit our test results and, in turn, receive an assessment report of our method performance against our peer's results. When a formal program is not available for some of our specialized tests, we create an internal assessment program with other laboratories that offer the same test, establish criteria for acceptance and monitor our performance. When a test result does not meet the predetermined quality criteria, the laboratory conducts an investigation to establish a root cause and implements corrective action to resolve the performance issue.

Patient Safety and Quality Assurance in Anatomical Pathology

Anatomical pathology is a science of interpretation. This means that in addition to pre-analytical quality measures such as patient and specimen identification, a quality assurance system should include proficiency testing through peer review. Cervical cytology testing was the first to implement proficiency testing back in the 1970's and 1980's, as a result of media coverage of flaws in cervical cytology reporting. Since then, a blinded review of 10% of all smears is performed by cytotechnologists of the same laboratory (6). Incongruent cases are to be referred to the chief cytotechnologist or cytopathologist.

Surgical pathology is a field with a much larger diversity in specimens and techniques and therefore implementation of similar proficiency testing has taken much longer to implement. Furthermore, manpower issues limit the extent of the review system. As of yet, there is no CAP (College of American Pathologists) standard for quality assurance in surgical pathology. Presently at HRLMP, a post-sign-out peer review of 1% of all specimens is performed.

Incongruent cases are to be discussed between the originating and reviewing pathologist and in cases where there is disagreement, external expert opinion is requested. The recent media coverage of flaws in quality of anatomical pathology has prompted the CAP/ACP (Canadian Association of Pathologists) to rethink current practices and propose nationwide guidelines. At the recent CAP Summit on Patient Safety and Quality Assurance in Anatomical Pathology (7), sources of errors and ways to avoid and correct them were reviewed. Errors occur in two categories, the first representing simple human mistakes and the second representing errors related to diagnostic competency. To address the first type of error, the review percentage would have to be increased, which would add significantly to the workload of pathologists. To address the second (diagnostic) type of error, expert peer review may be necessary within certain sub-specialization groups. In dealing with both types of error, the review should be performed before report sign out, in order to prevent harm to the patient.

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The laboratory report: (quality goal - an appropriate test interpretive guide)

Reference intervals for clinical chemistry tests

Laboratory test reports usually include a reference interval and the test result will be interpreted by comparison with these intervals. The quality of the reference intervals will play a large role in the result interpretation and any follow-up action. Setting reference intervals is done by following standard protocols. The *de novo* determination of any reference interval requires the recruitment of at least 120 healthy reference individuals in order to achieve an acceptably acceptable confidence in the reference range (8). This approach can be a significant undertaking in terms of time, resources and costs to the laboratory, so alternative processes for obtaining data may be considered. The data may come from the literature, other laboratories or provided by the manufacturer. Prior to adopting these reference intervals, it is validated in a small number (20) of healthy individual's representative of our patient population. This approach of transference is used by our laboratory for adult reference intervals.

As is well known, adult reference intervals are often not valid in pediatrics. Differences in physical size, organ maturity, body fluid compartments, (rates of) growth and development, immune and hormone responsiveness, nutrition and metabolism, are among the many factors that can influence normal analyte levels in children. Many manufacturers do not provide reference intervals for the pediatric population and many of our reference intervals are adopted from the literature. However, there are many gaps in the available data and to address this problem, our laboratory is participating in a national initiative for establishing reference intervals for the Canadian pediatric laboratories (CALIPER). The long-term aims of the CALIPER program are to establish age-specific and gender-specific pediatric reference intervals for both current and emerging biomarkers from neonatal age to adolescence (0-18 years of age in males and females) and to assess comparability/deviations among pediatric reference intervals in major ethnic groups representing the current Canadian diverse population.

At the other end of the age spectrum is geriatrics, a population which is increasing rapidly such that by 2015, Canada will have more people 65 years of age and over than young people less than 15 years of age. The heterogeneity of this population is greater than the younger adult group (18 - 65 years) because of increased use of medications, particularly for chronic diseases, acute disease, muted symptoms and age-related physiological and biochemical changes. There is a gradual decay of homeostatic mechanisms which increase the susceptibility of older persons to disease and decrease their ability to recover from them. Differentiation between age-related changes and disease-related biochemical changes is difficult and not well understood. The Canadian Longitudinal Study on Aging (CLSA), a national study on quality of life and health will follow 50,000 participants aged 45 - 85, for at least 20 years. Data from this study will be used to establish reference measures to interpret test results in older adults.

Conclusion:

There are many components to our Quality Management System. With the clinical staff and laboratory working together we have the ability to provide the right test analyzed by the best method and performed on the right patient and the correct result reported to the right people. Our goal is the promotion of evidence-based laboratory practices, and the continued development of mechanisms to improve quality of laboratory services will ensure – *Laboratory testing for effective patient care.*

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To provide a broad picture of our Quality Management System, this issue included contributions from all disciplines in the HRLMP program. Other contributors include:

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