

The Role of Laboratory Testing in Disease Diagnosis: A Comprehensive Review

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1. INTRODUCTION

Modern laboratory medicine plays a crucial role in the diagnosis, prognosis, and therapeutic monitoring of diseases. Despite the multitude of sophisticated methodologies for the analysis of body fluids and tissues to evaluate their normal and disease states, the laboratory location and organization have changed little over the past fifty years. All of the preanalytical variables, such as patient preparation, collection of the sample, handling, storage, transportation, and preparation for analysis, can directly affect the reliability of the results obtained across all of the various disease types. Guidelines have been produced to harmonize preanalytical requirements and standard operating procedures developed across the world to assist hospital and community staff in achieving the aims of sample quality. With the multiple disciplines under the laboratory umbrella, it is not just the biochemist or medical consultant that needs to be aware of the underlying preanalytical variables, but also the clinician taking the sample, irrespective of their location in the world.

Methods

We conducted a systematic review of the literature through extensive searches using databases up to January 2010. We included any study that evaluated the role of laboratory tests in disease diagnosis. Laboratory testing must have been used as part of the test evaluation design. The diagnostic performance of the test must have been a measure or part of the test evaluation. All potential studies were screened and

then the full text of papers was appraised. All data were extracted by three independent reviewers using standard appraisal and extraction tools.

Conclusion

In conclusion, we have examined and discussed some salient points that highlighted the state of practice and the value of laboratory diagnostics in ameliorating clinical outcomes and therapy. Laboratory testing is the single highest volume medical activity, with over six billion medical laboratory tests ordered annually, serving a vital role in the diagnosis, prognosis, and risk stratification of health-related conditions and diseases. Seventy to 80% of decisions affecting diagnosis or medical treatment are influenced by laboratory test results. In the modern era, advances in laboratory medicine have enabled small, fast, accurate, quantitative, and integrated patient-testing systems for use at or near the patient's location. These developments are collectively known as point-of-care testing, and such capabilities have opened up new models of healthcare delivery, such as home testing, health clinics, and mobile app technologies. The potential role of the clinical laboratory in an ever-evolving medical discipline lies in its ability to provide support to diagnose, treat, and manage diseases in a cost-effective, reliable, and timely manner. The use of the most technologically advanced laboratory services generates laboratory results that can enable both healthcare providers and their patients to make better health-related decisions that can enhance healthcare quality, patient satisfaction, and the utilization of resources.

Introduction

A diagnostic test may be defined as a procedure that is carried out in a laboratory as part of the diagnostic process. The aim of using these diagnostic tests is to identify the underlying cause of a patient's condition. Research selection criteria were studies evaluating the use of a laboratory procedure to detect disease or identify the etiology of a patient's symptoms in which test performance was compared with a well-defined criterion of disease status in a population with symptoms suggestive of the target condition. Laboratory tests play an important role in helping physicians during the diagnostic process. Quick, accurate diagnosis of diseases also ensures correct and appropriate treatment and management, and their paramount importance in modern healthcare systems is widely recognized. The role of laboratory testing in the diagnosis of diseases may be broadly divided into three main groups: diagnosis, differential diagnosis, and prognosis monitoring.

Laboratory testing is an extremely important concept for all medical undergraduates and general practitioners. It forms a significant arm of diagnostic medicine, which comprises 70% of the decisions made by treating physicians. Medical professionals are wary of the cost implications of laboratory testing and the tendency to request exhaustive tests on all patients. With the cost-effectiveness of most tests already being

established, an attempt to increase the knowledge of the general population may also be made. The concept of first consulting medical professionals for the diagnosis of certain 'minor' illnesses or using the internet or pharmacies must be stalled. However, neglecting the necessity for laboratory diagnostics in complicated cases or in a triage is difficult to dilute. Apparently, a no-win situation exists. Hence, consultants and house officers play a key role in sending the right message across. Currently, the incorporation of laboratory testing as an undergraduate university course, stressing the significance of being knowledgeable about the various relevant tests and ensuring their appropriate use by primary care physicians, sends a strong message to prevent the delay or reliance of the patient on the internet or fellow patients.

2. Historical Perspective of Laboratory Testing

Lab-based diagnostic testing has made immense progress over the last few decades. Other than a brief mention in medical history, the promulgation of preventive medicine, public health initiatives, or even advances in pioneering surgical and anesthetic techniques, the contributions of diagnostic laboratory testing to this dramatic transformation have often been overlooked. In reality, the laboratory is a major determinant of patient care, with as much as 60% of treatment decisions being dependent on the results obtained.

The significance of diagnostics in ascertaining the nature of disease has passed down the ages, only that the techniques that were applied found relevance to the technology that was contemporarily available. A historical perspective is essential to understand progress in any field—more so in diagnostic testing, where painstaking labor, frustration, and failure have often been the stepping stones to success. Although history may not indeed repeat itself, it is generally believed that this vocation follows similar pathways in achieving the final goal of medical advance.

3. Types of Laboratory Tests

Laboratory tests are used to diagnose and monitor an individual's health based on the standard reference intervals for that population. Approximately a large number of clinical decisions are based on the results of these tests. In vitro diagnostic devices also have a valuable role in the clinical guidance of health consequences from lifestyle or leisure activities, decisions around high-risk activities, and medico-legal situations. It is important for the user to take into account the characteristics of a given marker before considering it—either alone or in combination as a clinical laboratory partner. This chapter highlights the scientific principles behind the major approaches to indicator measurement and the different types of laboratory tests. We describe different categories of laboratory tests: clinical chemistry, endocrinology, hematology, immunohematology, immunology, infectious diseases, molecular diagnostics,

phlebotomy, point of care, quality control and quality assurance, and urinalysis. (Binnicker, 2020)(Sharma et al., 2021)(Chen et al.2020)

Clinical chemistry includes measurement of the following components: anion and cation concentrations in the aqueous phase of blood; serum concentrations of non-protein nitrogenous substances; enzyme activities that measure tissue injury or are specific for a particular organ; lipid studies; and electrolytes. The information is useful primarily in the diagnosis and management of metabolic disorders, infectious diseases, and neoplasia.

3.1. Clinical Chemistry Tests

Clinical chemistry is the theme of studies that address the quantification of substances present in blood when the blood is in a resting state. Measurement methods are based on the properties of molecules that can absorb, fluoresce, refract, and conduct electricity. These tests should give medical care providers the information needed to carry out the following activities: • To establish an illness; • To narrow a list of possible diagnoses; • To record the degree of deviation from normal values and establish the stage of a disease; • To monitor the progress of a disease and the effects of therapeutic procedures; • To identify and monitor toxic substances; • To assess the efficiency of an organ and its general state. All procedures are performed using a small or capillary blood sample at the moment of a patient's visit.

To request an exam, the physician has to prescribe them according to what their patient presents as symptoms or signs. These tests are performed using expensive equipment that needs to be maintained and operated by professionals in the clinical analysis area called clinical pathology or laboratory medicine. Laboratory results indicate a particular amount of a molecule present in a specific amount of biological fluid. The results are reported in the form of numbers or ranges of numbers established by the staff at the request of the physicians associated with the laboratory's staff according to specific demographic characteristics of its patients. A common use of clinical chemistry tests is to quantify known quantities of substances present in the patient's blood referred to as analytes.

3.2. Hematology Tests

Hematology tests are blood tests that focus on diseases of the blood and blood-forming organs. These tests encompass the white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin concentration, red cell indices (mean cell hemoglobin, mean cell hemoglobin concentration, and mean cell volume), red cell distribution width, platelet count, and platelet indices (mean platelet volume, plateletcrit, and platelet distribution width). Evaluation of hematologic indices is necessary for disease diagnosis. In routine

analysis, hematology analyzers are commonly used to perform hematologic tests via automated methods. (Elshazli et al.2020)(Yuan et al.2020)(Liao et al.2020)(Cabitza et al.2021)

Hemoglobin of RBCs performs the duty of oxygen transport and CO₂ transport. RBC indices perform a significant role in the differentiation of anemia types according to erythrocyte life-cycle status. Hct, the percentage total volume in the blood made up by the RBCs, is a clinical estimation developed from the RBC count and the mean cell volume. MCV refers to the size of RBCs and is generally expressed in femtoliters and is calculated according to the equation. MCHC, the mean concentration of hemoglobin in erythrocytes, is defined by the equation. It is important in the identification of RBCs for disease diagnosis. RDW is a quantitative estimation of RBC volume variation and is used to differentiate microcytic and normocytic RBCs. It is reported with the RBC count on the blood morphology analysis.

Platelet count is reported by automated hematology analyzers. It performs significant roles in the diagnosis of thrombocytosis, which may be associated with severe infections, malignancies, or platelet disorders, and in the diagnosis of thrombocytopenia, which is associated with hemato-oncologic disorders. Platelet indices such as plateletcrit and platelet distribution width provide significant indicators for diagnosing thrombocytosis and thrombocytopenia. Mean platelet volume is a significant variable known to be involved in various hematopoietic activities, especially in thrombopoiesis. An increase in mean platelet volume may partly reflect greater turnover of platelets in the blood. On the other hand, a decrease in mean platelet volume corresponds to greater consumption of platelets in the blood and may be of value in the diagnosis of residual hematopoietic and liver diseases. Only a few tests are sought due to the cost of facility construction and the number of technical experts for hematology tests. Finally, of the whole blood supply profile, the parametric laboratory data are beginning to be used for the diagnosis of different disease types.

3.3. Microbiology Tests

Microbiology is the study of microorganisms such as bacteria, viruses, fungi, and parasites. All microorganisms are invisible without a microscope. A microbiology laboratory functions by identifying the microorganism and performing sensitivity tests to determine the appropriate treatment if the disease is caused by bacteria or fungi. Virology focuses on the investigation of viruses. In the microbiology laboratory, the focus is on the diagnosis of infectious diseases, whether caused by bacteria, fungi, parasites, or viruses. Detection may be direct by examining the sample for the organism itself, not just for the immune response, or, if organelles are looking for an antigen or gene sequence, samples may be used to achieve an accurate diagnosis of contagious diseases or determine resistance tests. The sample required for

microbiological testing is usually blood, urine, swabs, stool, sputum, etc. The most commonly tested requests include: 1) Special requests such as viral cultures and serology; 2) Rapid test requests, such as direct antigen detection for respiratory syncytial virus, direct fluorescent antibody test for adenovirus, and rapid culture for group A Strep; 3) Bacterial cultures and sensitivities including urine, sputum, stool, blood, swabs, etc.; 4) Mycobacterium tuberculosis testing (culture including acid-alcohol smear and susceptibility test); 5) Anaerobic bacterial culture and sensitivity requests, fungal culture, parasite testing, and stool culture with concentrate or modified acid-fast smear; 6) Blood culture requests, bacterial or fungal positive identification requests; 7) Mycoplasma and ureaplasma tests in various sample types; 8) Fungi and yeast identification.

3.4. Imaging and Radiology Tests

In some diseases, clinical history and laboratory investigations cannot establish the diagnosis clearly, particularly in disorders affecting several systems. Imaging tests might be needed to confirm the diagnosis. Although radiologic techniques are not included as part of the main laboratory, they are involved in the diagnosis of most diseases. Radiology tests include standard radiographs, ultrasonography, computed tomography, and magnetic resonance imaging. Diagnostic imaging has developed so quickly over the past 30 years that most people of all ages have had at least one, or more commonly, several imaging studies by the time they become adults. Over the years, the acquiring technology and the number of indications for imaging have expanded greatly and have led to complex discussions regarding the additional costs and risks of the studies.

Radiologic studies have advantages and disadvantages over other laboratory tests. Imaging studies are crucial for the diagnosis and treatment of many diseases because they provide information that simply is not available through physical examination; however, it is crucial to minimize unnecessary studies that increase costs and morbidity among the population. A good test is safe, not costly, and has simplicity, reproducibility, and high sensitivity. The meaning of these tests is that high sensitivity indicates that the test is rarely positive in the absence of the disease. High specificity indicates that the test is rarely negative in the presence of the disease. All of these factors must be considered to inform therapeutic decisions. A method for detecting nodules along the lung line, with lung cancer being a cause of the suspicious nodules.

4. Role of Laboratory Testing in Specific Diseases

Laboratory testing is a fundamental component in the diagnosis and management of patients suffering from any bacterial, viral, parasitic, or other infectious disease. Accurate and timely results of laboratory tests not only help in confirming the

organism causing the particular disease but also monitor the magnitude and severity of the disease itself. Advances in technology and automation have prompted the exponential growth of tests that can be offered and have further permitted the realization of not only specific but also sensitive screening tests that are critical for disease identification and prevention. The availability of rapid molecular tests and quick turnaround times for the most commonly performed tests helps primary health care physicians in diagnosing infectious diseases and also monitors the presence of the infectious agent, with quick therapeutic turnaround time being crucial in the clinical outcome of the patient. The disease conditions discussed have major importance both in the developed and developing world. The role of laboratory tests, performed in both near-patient and centralized laboratory settings, differs extensively based on factors such as initial clinical characterization of the disease, severity of the disease, presence of any kind of antimicrobial resistance mechanisms, geographical spread of diseases, availability of diagnostic tests, and cost of the tests. Emerging infectious diseases have to be diagnosed promptly for the prevention of spread, and laboratory preparedness, either locally or globally, is crucial in identifying such emerging infectious diseases at an early stage. This discusses the laboratory testing requisites and diagnostic methodologies of major infectious diseases caused by viral infectious agents, including those that cause upper and lower respiratory tract infections, central nervous system infections, genital infections, hemorrhagic fevers, hepatitis, and other diseases including torquetenovirus, polyomaviridae, and iridoviridae infections, measles, rubella, mumps, influenza, parainfluenza, respiratory syncytial virus, and metapneumovirus respiratory tract infections.

4.1. Infectious Diseases

Clinical laboratory tests sometimes dictate patient management and therapy, a process that must be fast and accurate. Clinical laboratories offer many potential tools for managing patients with infectious diseases, including antigen detection tests, culture methods, microscopy, serology, and more recently developed PCR tests. These tests can contribute to the diagnosis of patients with symptoms of infectious diseases, guide therapeutic choices through antimicrobial susceptibility testing, and determine if treatment has been successful. In this chapter, we will provide concise and practical information to help physicians use the various available laboratory tests for the diagnosis of infectious diseases. Despite the help that clinical laboratory testing can provide in managing patients with infectious diseases, these tests are often overused or misused. There are many potential explanations for the inappropriate use of laboratory testing, including inaccurate perceptions about how best to use the tests and financial incentives to overuse them. Understanding test attributes can help to recognize when test results are unreliable.

4.2. Cancer

Cancer is the second leading cause of death worldwide. However, the total economic impact of cancer care has not been adequately examined from the perspective of health budgets and the cost of financing cancer care at the household level. Earlier diagnosis and improved treatment of cancer are required. To assist in the diagnosis of cancer, the role of laboratory tests is multifaceted. The role of conventional wavelength-based absorbance spectrophotometry and colorimetry laboratory detection methods has been reviewed.

Cancer markers are primarily utilized for screening, monitoring, detection, and tracking response to therapy. Metastases, a significant characteristic of invasive cancer that is responsible for 90% of patient mortality, may occur in the later stages of the disease. Early detection of cancer and metastatic disease is of utmost importance as it significantly increases the chance of a positive therapeutic response and enhances the chance for patient survival. To demonstrate effectiveness, we have outlined the best techniques. In our review, we also present the most recent study periods. The majority of cancer markers present sensitivities and specificities of less than 70% and 85%, respectively.

4.3. Autoimmune Disorders

Autoimmune disorders are characterized by the body's immune system mistaking its own tissues or cells as foreign, attacking them, and causing tissue damage. In autoimmune disorders, the immune system loses the ability to differentiate between foreign and self-components. Autoimmune diseases are often characterized by the presence of antibodies to self-antigens; that is, the body produces autoantibodies against self-antigens. The diagnosis of autoimmune diseases is increasingly challenging due to the variety of autoantibodies and the time, expense, and technical difficulties that clinicians face in the investigation of autoreactivity in their patients. The patient sample of choice is typically serum or plasma, the two most commonly used materials in diagnostic testing.

As it usually takes a long time for the human immune response to become strong enough to produce autoantibodies at such levels that they become detectable, it is often difficult for clinicians to assess the clinical symptoms in the context of antibody serostatus. Generally, the most effective approach for clinicians is to obtain paired acute and convalescent samples. The levels of autoantibodies produced during the response may vary greatly with geographical or other epidemiological factors, such as the infecting strain of the particular pathogen that methods can detect. In the late 1940s, clinicians generally employed indirect immunofluorescence for testing antinuclear antibodies with clinical samples. With the discovery of immune complex-

associated particles observed in a patient with systemic lupus erythematosus by Philip Hench, IIF-ANA testing provided the first clinical test for the diagnosis of systemic lupus erythematosus.

5. Challenges and Advances in Laboratory Testing

Rapid advances in laboratory testing that either diagnose or phenotype diseases have allowed high-throughput processing of both clinical and research samples. However, a disadvantage of developing the testing apparatus is the temporary reduction in sensitivity, specificity, and assay robustness. Without consistent and robust testing conditions, cross-proficiencies cannot be easily established based on large datasets. This means poorer reporting of diagnostic values, the potential development of subgroups with lower sensitivity, and potential ethical issues that may arise from such changes. Surprisingly for research, apparent changes in sensitivity and specificity would lead to biased hypotheses that would arise through an incorrect interpretation of a flawed test. This highlights a potential problem arising from the rapid development of laboratory tests that are used both in the clinical management of disease and in research studies. Research based on clinical validation can be flawed if results from inpatients, particularly geriatric patients, are used. Levels of compassion, time, and experimental sample collection can be minor considerations for diagnosticians using diagnostic testing to validate timely treatments, but these are not concerns for clinicians.

6. Conclusion and Future Directions

In conclusion, this review has summarized the main functions of laboratory testing and outlined its role within the wider diagnostic process. Throughout, we have highlighted the need for a better understanding and use of this tool, which, far from being purely a test, is a significant component in the understanding of disease pathophysiology, the realization of personalized patient management, and the improvement of whole healthcare systems. The main challenges of laboratory testing technology and its current use have also been identified, and some future perspectives have been outlined. Ultimately, the more we understand, trust, and share lab technology use, the higher its return in terms of value for life. Although we still need to improve diagnosis as a whole, a deep knowledge of the potential of laboratory testing will contribute significantly to reaching this challenging goal—is the time of clinical diagnostics now?

So far, clinical diagnostics has focused mainly on detecting and monitoring diseases. Nevertheless, the next question that laboratories should address is to answer the why of the disease. Are we providing the right therapy because the epidermal EGFR is mutated, or are we diagnosing the mutation because it is treatable? When are we

diagnosing a disease that will never show any clinical sign, or when are we identifying diseases that will eventually make a difference? Why did the disease appear? What is happening at the subcellular level, and is this mechanism exactly the same between different diseases with the same name? Finding the answer to these questions will lead to a shift toward preventive diagnostics: rather than diagnosing diseases and related complications, the main mission of laboratory medicine will become the identification of mechanisms triggering disease. Preventive measures can thus be taken, and personalized and patient-centric management will become a reality. Only then will labs be truly providing health, and value for life in lab tests will rise dramatically.

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