Strengthening diagnostic capacities for Zoonotic Diseases in India

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Abstract

Preventing and controlling zoonotic diseases requires coordination among various national, regional, state, and local stakeholders in the health, veterinary, and wildlife departments. These stakeholders rely on each other for laboratory diagnosis and timely response. Unfortunately, there is a lack of standardized procedures and approved kits for diagnosing these diseases, which limits laboratory capacity for diagnosis. Additionally, limited technical expertise and the absence of internationally recognized EQAS agencies further complicate the diagnostic process. Therefore, it is crucial to prioritize zoonotic diseases that require a laboratory network and integrate them at the veterinary and human levels based on focus areas outlined in this manuscript. This article offers a roadmap for developing policies for each prioritized zoonotic disease using the 4C model (Communication, Coordination, Collaboration, and Capacity building) of One Health.

Keywords: Zoonoses, One Health, capacity building

Introduction

Classical infectious diseases like rabies and plague, well known for centuries, are zoonotic infectious diseases that have not been eradicated despite significant efforts from human and veterinary health sectors. The zoonotic diseases of major public health importance in India are Dengue/CHK, Japanese encephalitis, leptospirosis, plague, rabies, anthrax, Kala-azar, Kyasanur Forest Disease, Rickettsial diseases, cysticercosis, hydatid disease, trypanosomiasis and toxoplasmosis, some of which cause outbreaks at a great frequency.

Recently, new zoonotic entities with pandemic/ outbreak potential in humans such as Monkeypox (2022) and SARS-COV-2 (2019 onwards), Crimean Congo Hemorrhagic fever (2011 onwards), Nipah virus infection (2001 onwards), Ebola virus (2014 onwards), Avian Influenza (2006 onwards) & H1N1 Influenza (2009 onwards) have stirred the public health machinery. Apart from these, the country is threatened by the import of exotic zoonotic infections like Yellow Fever, Hantavirus infection, Rift Valley fever, etc. The infections/diseases, as evident, can travel across the world and result in not only loss of human and animal lives but also devastating effects on economies. As the disease transcends beyond more than one species, the approach to protecting lives from these infections also is multidimensional, involving many Stakeholders.

One Health is an integrative approach that aims to achieve active participation from all the stakeholders. One Health requires all the stakeholders from human, veterinary, and environmental health to come together and address the health challenges and issues. One Health High-Level Expert Panel (OHHLEP) was established under a quadripartite collaboration between Food and Agriculture Organization (FAO), World Health Organization (WHO), World Organization for Animal Health (WOAH), and United Nations Environment Programme (UNEP) has defined one health as follows [1]:

"One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent. The approach mobilizes multiple sectors, disciplines, and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems while addressing the collective need for healthy food, water, energy, and air, taking action on climate change and contributing to sustainable development."

The definition emphasizes a 4C model based on Communication, Coordination, Collaboration, and Capacity building to transform OH from a concept to reality. Defining OH in this way is a milestone as it identifies equity, parity, equilibrium, stewardship, and trans-disciplinarity as critical underlying principles for OH. The present manuscript aims at identifying focus areas for strengthening diagnostic capacity for zoonotic infections and employ the 4C model for developing a policy framework for implementation.

As a policy framework, the present text does not include sections on policy analysis, including budgetary provisions, as it is outside the purview of this manuscript. The policy framework for focus areas for diagnostic capacity strengthening are outlined in Figure-2.

Challenges posed and proposed solutions based on one health approach for each focus area will be discussed in the subsequent sections of this manuscript. As different zoonotic infections will have specific requirements in terms of diagnosis, this framework will need to be used for developing policies for each zoonotic infection on a case-by-case basis based on expert consultation.

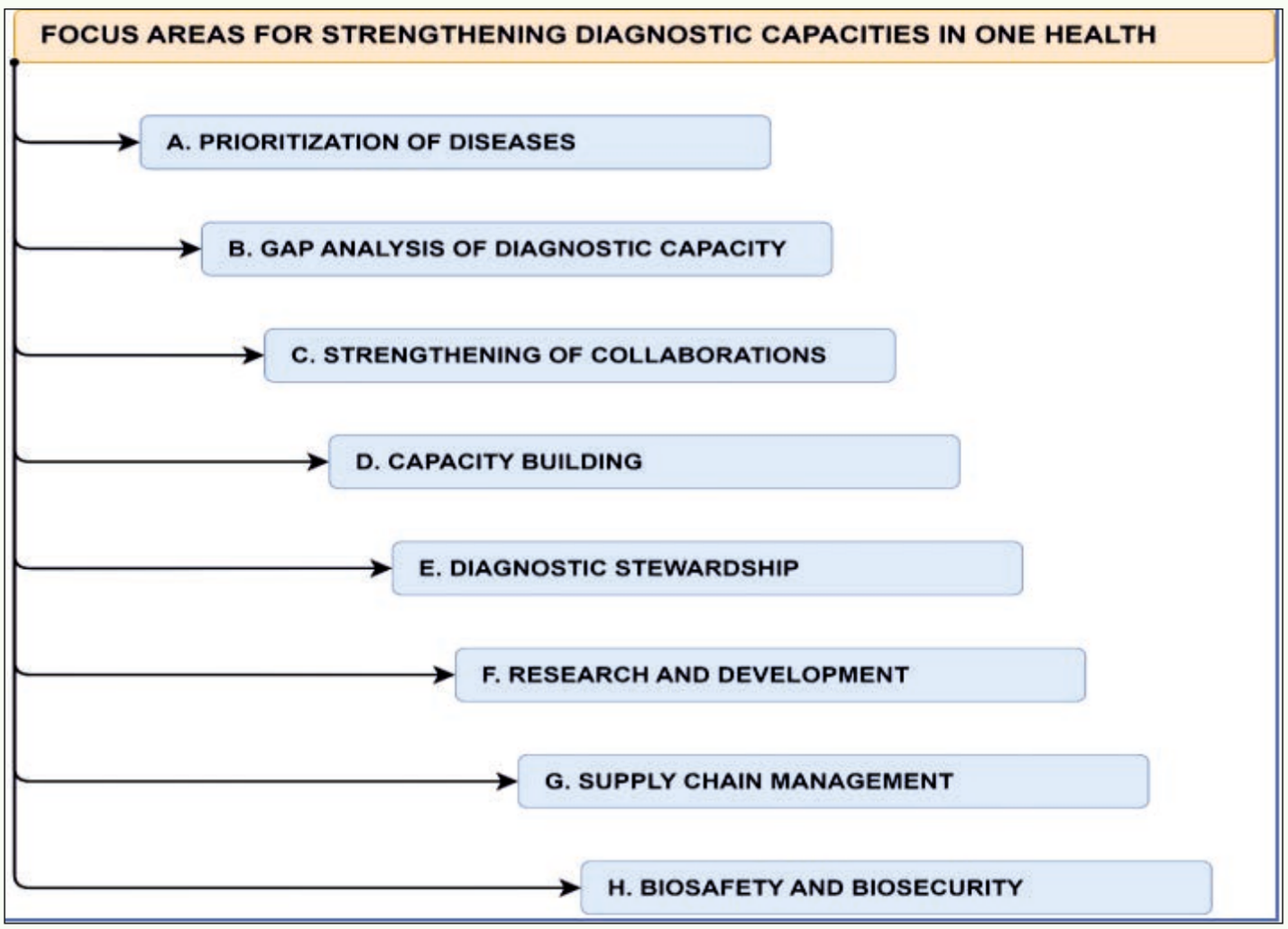

Figure 1: Focus areas for strengthening diagnostic capacities in one health

Strengthening Diagnostic Capacity in One Health

A. Prioritization of diseases:

The foremost issue to be resolved for initiating any OH-based approach is prioritizing the diseases. As a concept, OH should encompass all the diseases that humans and animals share. In practice, however, the system must be systematically strengthened to ensure the OH approach's success. The prioritization is a collaborative task and requires a multi-sectoral consensus-building effort of experts from various stakeholders. The criteria for prioritization of diseases can be defined based on the following factors with expert consultation [2].

1. The severity of human disease
2. Role of animals in human diseases
3. Availability of therapeutic intervention
4. The burden of animal disease (endemicity)
5. Any existing intersectoral collaboration

B. Gap analysis of diagnostic capacity:

The immediate step after prioritization of disease is to understand the diagnostic capacity of India for each disease. Gap analysis, again, is a multi-sectoral exercise and involves identifying diagnostic gaps in the country across the sectors. Two broad areas considered for gap analysis are:

1. Diagnostic capacity mapping – the diagnostic capacity can be mapped to identify laboratories performing diagnostic tests in human and veterinary sectors, availability of equipment and infrastructure, list of available diagnostic methods (preferably with

their diagnostic performance characteristics), and workforce competency.

2. Diagnostic quality mapping – the diagnostic quality can be mapped regarding quality control and quality assurance protocols followed by the laboratories, including participation in any External Quality Assurance (EQA) programmes or inter-laboratory comparison (ILC) programmes.

C. Strengthening of collaborations:

OH, as a concept, relies on collaborative efforts from various sectors. The strength of collaboration can be defined as the relative ease with which different sectors can work together to achieve a common goal. In the case of diagnostic capacities, the primary goal will be to provide services for surveillance, preparedness, and response for prioritized diseases. The gap analysis will provide information about areas where strengthening is required.

Collaborative efforts must engage all stakeholders to build up a successful collaboration. The nature of collaborative effort can have a significant effect on its success. Collaboration can be classified into four levels based on the extent of involvement between the sectors [3]. These levels are outlined in Figure 2 and are as follows:

1.Sectoral contributions:

Various stakeholders are working in their respective fields. There is no issue-based consensus or defined common goals between the sectors. Sectoral contributions from the baseline of response to any public health concern in the community.

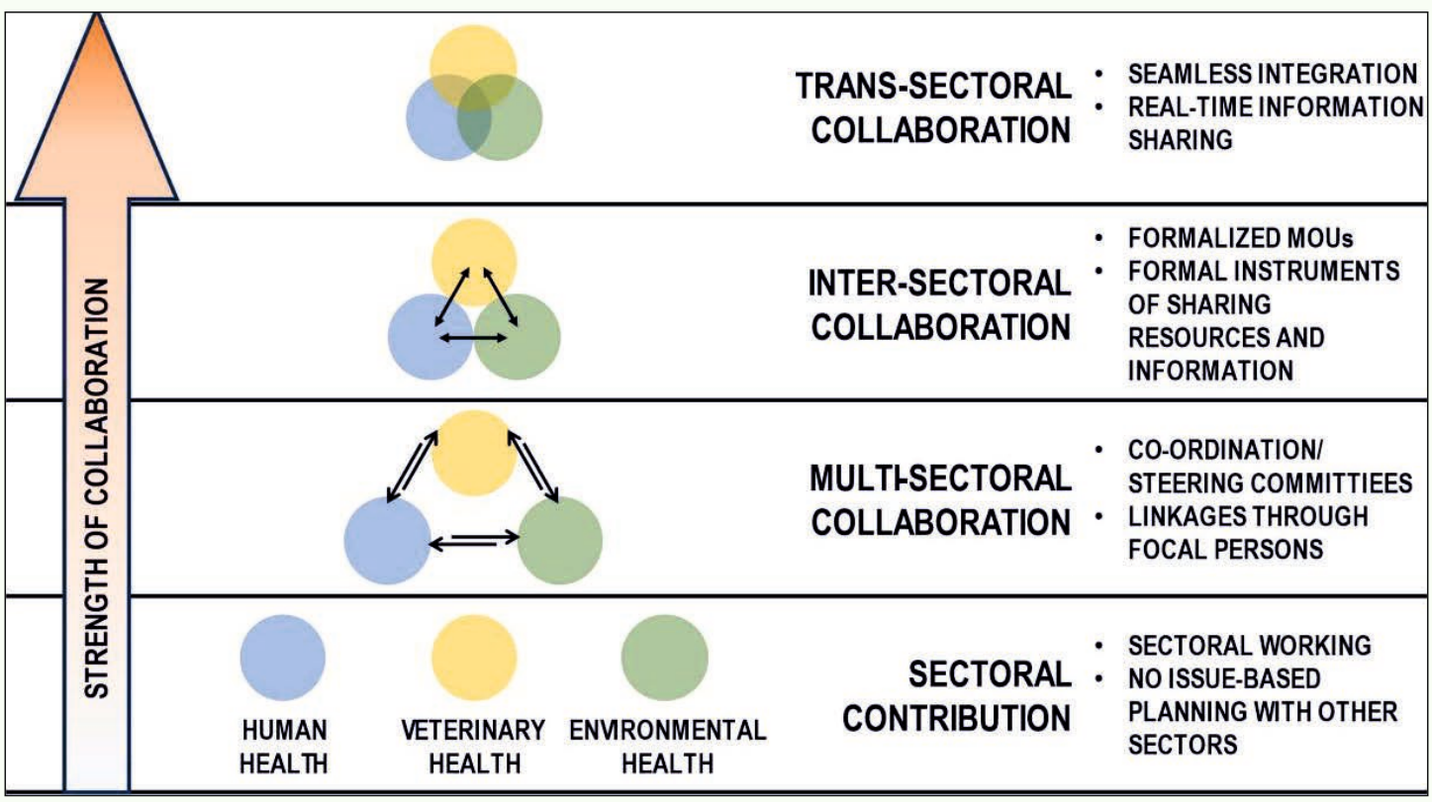

Figure 2: Concept of strengthening of collaboration in One Health [3]

2.Multi-sectoral collaboration:

Various stakeholders are working through coordination and steering committees, which are mandated to identify common goals and establish linkages between sectors by identifying focal points. Achieving this level is crucial for developing communication channels between the sectors.

3.Inter-sectoral collaboration:

Various stakeholders have agreed on common goals, have formalized the collaboration through memorandums of understanding (MOUs) between the sectors, and have developed resource and information-sharing instruments. Achieving this level is essential for capacity building.

4. Trans-sectoral collaboration:

Seamless integration between sectors to achieve a common goal and real-time information sharing. This level is essential for coordinating rapid response during a public health emergency.

Further, various factors may contribute to the success of a collaboration. These determinants of successful collaboration can be classified under three broad categories: individual attributes, environmental attributes, and procedural attributes [4]. In case of strengthening of diagnostic capacity, the determinants of collaborative success can be outlined as follows:

i.Personal attributes: Personal attributes ensuring successful collaboration include the expertise of the focal person or collaboration contact points in the organization, the relevance of their experience to the goals of collaboration, their ability to carry forward collaboration in a productive manner, and their motivation to be a part of the collaboration.

ii.Environmental attributes: Environmental attributes of collaborative success include institutional support regarding the infrastructure required and financial support in running the programme. These attributes are also enabling and may help provide motivation and collaborative skills in the persons involved.

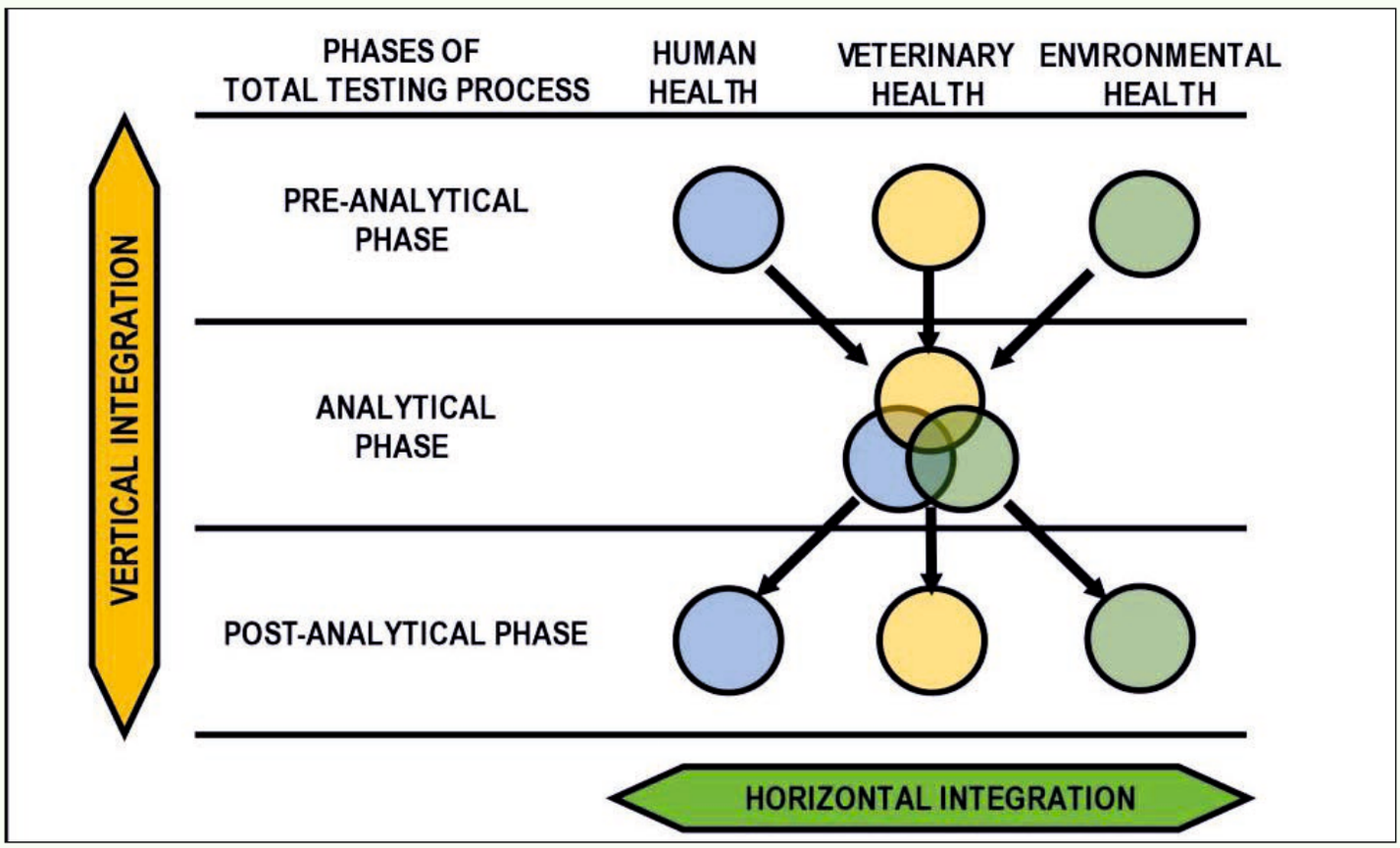

Figure 3: Capacity building measures for strengthening the diagnostic capacity in One Health.

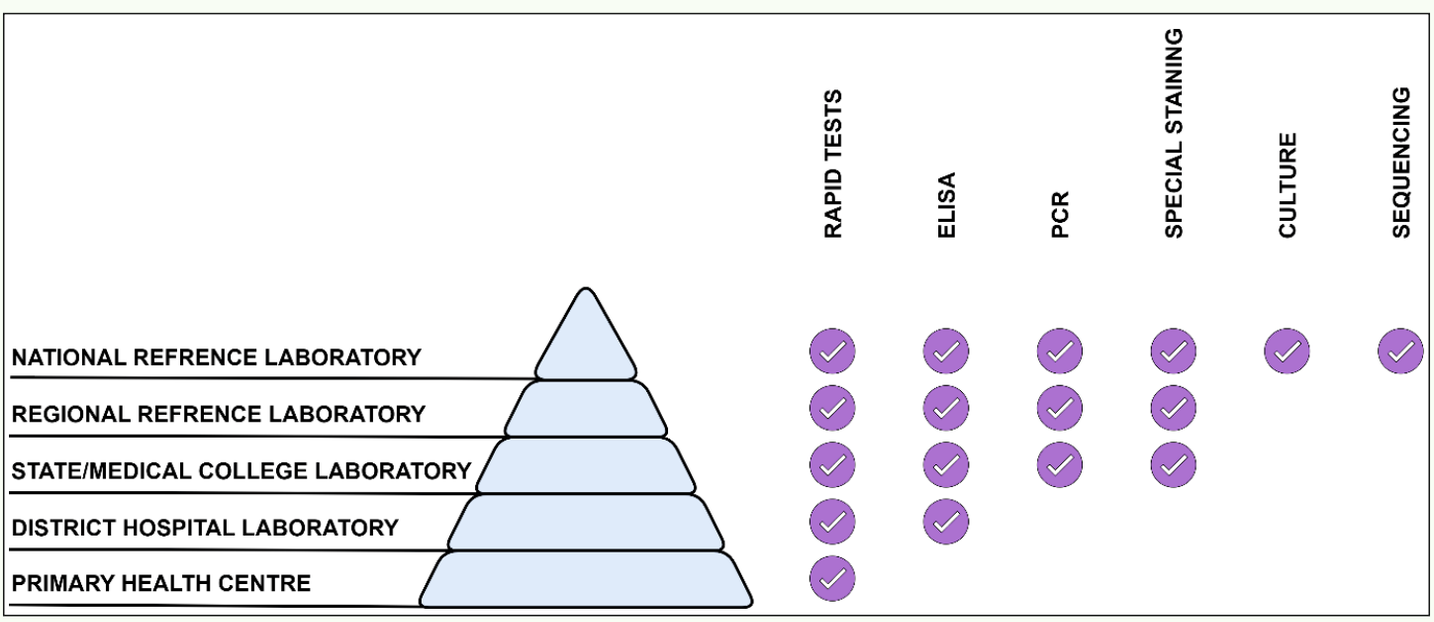

Figure 4: Tiered laboratory network mapped to available tests and competency of the staff at each level. (Example-Laboratory network of Rabies)

iii.Procedural attributes: Procedural attributes may include formalizing the collaboration through signing MOUs, developing a common goal such as strengthening laboratories for diagnosing a particular disease, regular communication with all stakeholders regarding the common goal and progress made, and establishing conflict resolution mechanisms through formal instruments like MOUs. Formalization of the collaborative process results in developing a shared responsibility and providing a conflict resolution framework while preparing academic manuscripts or sharing the credit among the stakeholders.

D. Capacity building:

The capacity building exercise aims to develop the overall ability of the system to detect, diagnose, and characterize pathogens causing diseases in a particular geographical area. The capacity building exercise requires understanding of various steps in the total testing process (TTP). TTP includes pre-analytical, analytical, and post-analytical aspects of a diagnostic test. It is essential to understand that errors in diagnostic tests span the entire TTP and are not limited to a single step [5]. By an estimate, the analytical phase had only 15% of errors during reporting, while the pre- analytical phase had 61.9% errors [6]. Therefore, it is essential to put a concerted effort to identify the human resource responsible for the successful completion of each step and put efforts to minimize the error by using appropriate capacity-building measures. Briefly, the following capacity-building instruments can be utilized to strengthen the diagnostic capacity in OH:

1.Advocacy workshops: Aim to inform clinicians about the appropriate test based on the patient's clinical symptoms, the optimum sample based on the disease stage, and available clinical management guidelines.

2.Guidelines: Guidelines about sample collection, storage, and transport need to be developed for each diagnostic assay and should be prepared in a language that is easy to understand.

3.Hands-on training workshops: Hands-on training workshops should aim to increase the proficiency of laboratory personnel in sample processing and testing.

In the context of capacity-building measures for strengthen diagnostic capacity may adopt vertical or horizontal integration approaches (Figure 3).

1. Vertical-integration model: Laboratories already engaged in analytical methods for other diseases can be targeted for vertical integration of new assays. The capacity-building measures should target all phases of TTP irrespective of laboratory experience.

2. Horizontal integration model: Horizontal integration involves sharing of resources across sectors. In the case of OH, laboratories from the animal and human sectors may be tasked to perform the analytical phase of the diagnostic assay. However, as the requirements for pre-analytical and post- analytical phases will vary for different sectors, these phases should not be integrated horizontally. For example, a veterinarian should not prescribe the test to a human

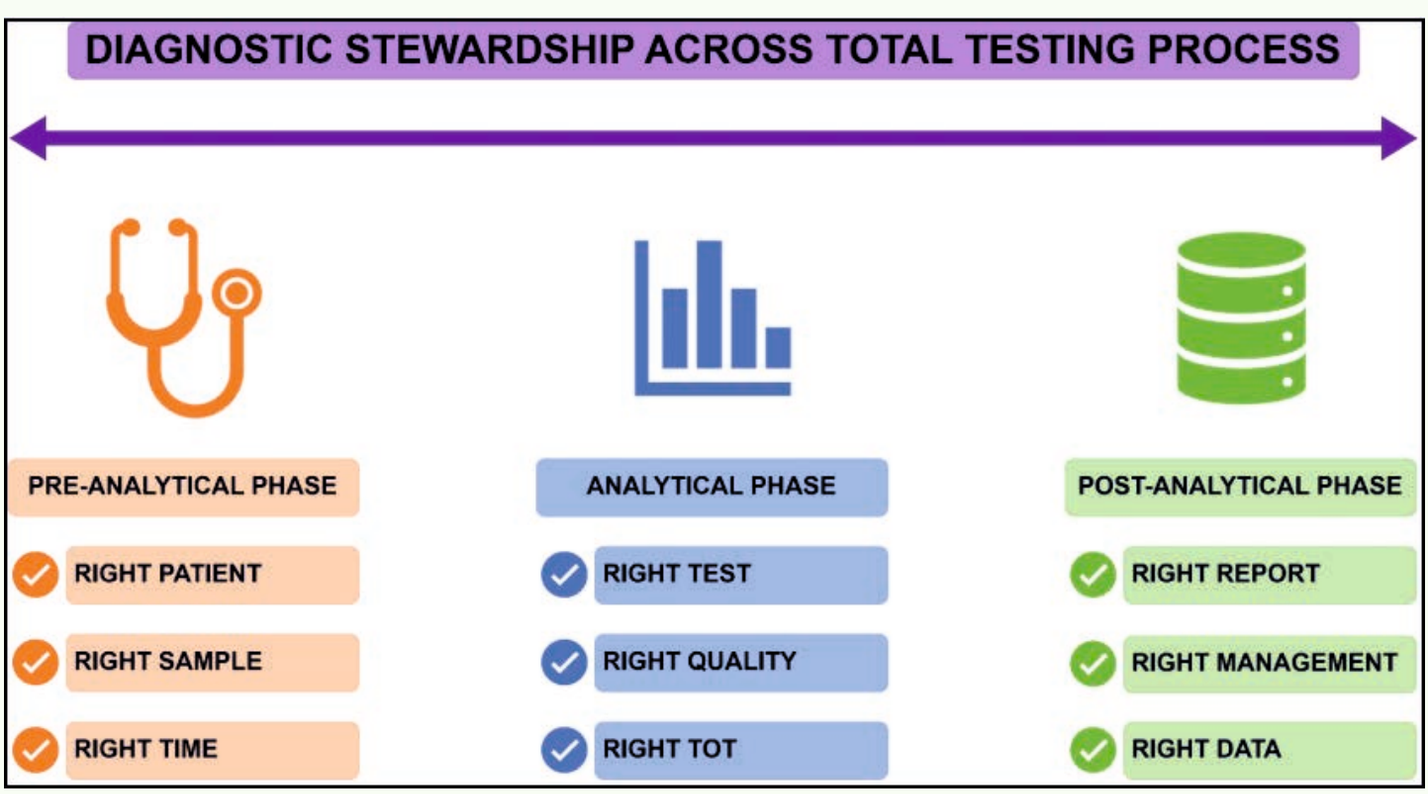

Figure 5: Diagnostic stewardship applied across the total testing process. Areas of focus has been identified for pre-analytical, analytical, and post-analytical phases.

sample, but a veterinary laboratory can perform the assay and report the results through established channels to clinicians for further action. Further, capacity building should focus on developing a tiered laboratory network while considering the staff competency available at each tier. A tiered laboratory network (example laboratory network of Rabies) is mapped to the diagnostic methods and competency of staff available is given in Figure 4.

E. Diagnostic stewardship in strengthening the diagnostic capacity in one health

Stewardship is a concept applied to improve diagnosis in healthcare based on the principal of minimizing diagnostic errors [7]. In a broader sense, diagnostic stewardship can be used to minimize errors across the total testing process. Championing diagnostic stewardship could provide appropriate clinical management and help control systemic issues in healthcare, such as antimicrobial resistance. In the context of strengthening diagnostic capacity in one health, diagnostic stewardship across the Total Testing Process (TTP) is shown in Figure 5.

Briefly, the focus areas during the entire TTP are as follows:

1. Pre-analytical phase: The focus of diagnostic stewardship in the pre-analytical phase should be on informing clinicians and sample collectors about the laboratory tests available and the requirements of laboratories to ensure that quality sample reaches for the testing [8]. In addition to sample requirements, the pre-analytical phase should also focus on packaging, transportation, and sample identification in the laboratory [9].

2. Analytical phase: The focus of diagnostic stewardship in the analytical phase should be on diagnostic laboratories. It is essential to understand what sample should be collected and when. Understanding the prioritized disease's pathophysiology and the kinetics of various diagnostic markers will help address this issue. For example, in dengue, understanding the dynamics of the appearance of viremia, antigenemia, anti-dengue IgM antibodies, and anti-dengue IgG antibodies can help select appropriate test [10]. The focus should also be on the analysis of the results as errors in analysis can result in inferior quality of reporting. Providing quality diagnostic assays is the mainstay of laboratory strengthening efforts.

ISO 15189 outlines the requirements of the quality management system in a diagnostic laboratory. NABL is the authority in India that accredits laboratories after verifying their compliance with these requirements (Document number NABL112). The ISO 15189 standard also requires establishing quality assurance in the medical laboratory. Laboratories can employ internal quality control (IQC) and external quality assurance (EQA) as the main tools to ensure and improve the quality of analytical methods through constant monitoring, evaluation, and improvement [11].

3. Postanalytical phase: The focus of diagnostic stewardship in the post-analytical phase is on developing guidelines on reporting results, undertaking advocacy workshops to inform clinicians about how to interpret the results, and ensuring that the data is being used to generate evidence for future improvement in control and management of the prioritized disease.

F. Research and Development

Focused research is required to establish diagnostic protocols for prioritized diseases, and effort should be put into developing these protocols as commercial kits through Public Private Partnerships (PPP). Developing disease-specific Target Product Profiles (TPP) remains the best instrument to persuade stakeholders to do focused research and development. TPP ensures the assays are developed to fit the intended purpose [12]. TPP requires extensive consultation to determine the scope of TPP, including any unmet clinical needs, drafting of TPP to include end user-specific requirements and consultation among stakeholders to reach a consensus [13]. TPP can be used as guiding document by public and private partners to develop required assays. Further, assay developed by academic institutions can be used as emergency diagnostic assays after proper analytical validation. However, using a commercial kit as an invitro diagnostic kit will require regulatory approvals.

G. Management of supply chain

Supply chain management remains a significant bottleneck for the diagnosis of zoonotic infections. Non-availability of commercial kits and unregulated pricing make managing supply chains unpredictable. Logistics management requires focusing on the following areas[14] :

1. Product selection: Product selection will depend on the type of assay required for prioritized diseases.

2. Forecasting: Quantification depends on the forecasting of the number of assays required to be performed in the coming year. Previous year baseline data, if available, can help in forecasting the number of tests that the laboratory will perform during next year. A proportional increase may also be estimated if yearly data for the last five years is available with the laboratory.

3. Procurement: The procurement process should consider the government procurement rules and availability of good quality commercial kits for the prioritized diseases in local and international market.

There may be a need to reverify the manufacturer's claims to ensure that the kits perform their intended function.

4. Inventory management: Inventory management of procured items, their distribution, and collecting consumption records may help minimize resource misutilization.

H. Biosafety and Biosecurity

Most pathogens causing zoonotic infections are also a biosafety and biosecurity concern. The biosafety measures must include the following attributes:

1. Monitoring and warning. A comprehensive monitoring system may be established employing both active and passive surveillance for prioritized diseases. Additionally, real-time information sharing mechanisms among all the stakeholders must be established enabling prompt response to an adverse incident.

2. Detection and traceability. Detection of pathogens and establishing their traceability through molecular methods may help identify the source of the breach in the system, thereby facilitating necessary improvements to prevent future incidents.

3. Prevention and control. It is essential to establish guidelines to inform laboratory personnel about the prevention and control strategies for prioritized pathogens which should be employed to ensure containment of any adverse event in the laboratory itself.

4. Diagnosis and treatment. Comprehensive guidelines should be provided regarding clinical symptoms, diagnosis, and available treatment of prioritized diseases. Such information may be pivotal in effective management of laboratory infections caused by prioritized disease.

5. Training and competency. Laboratory personals should be trained regularly in biorisk management, biosafety and biosecurity in public health laboratories to enhance their competency.

Competent staff will ensure prompt identification and containment of any adverse incident.

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Conflicts of Interest

None.

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