

Chapter 11

High-Quality Diagnosis: An Essential Pathology Package

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INTRODUCTION

A young child living in Sub-Saharan Africa presents to a rural health care clinic with a one-week history of fevers, night sweats, chills, and malaise. The child's mother does not know if the child has lost weight in the recent past; when weighed, the child is significantly below the expected weight for her age. No other family members, including other young siblings, report similar symptoms. Physical examination reveals a fever, mild increase in heart and respiratory rates, and enlarged lymph nodes along both sides of her neck. The clinic does not have access to imaging studies, and the only available pathology laboratory tests show that the patient does not have serologic evidence of human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) infection or malaria. She is mildly anemic as measured by a manual spun hematocrit. The physician wants to refer the patient to a hospital in a nearby city, but the family does not have sufficient resources.

The physician offers to collect blood for pathology testing and send it to that hospital for testing, but because the hospital requires advance payment for pathology tests, the family again does not have the resources. The physician completes the notes, indicating that the differential diagnosis is broad—including tuberculosis, nontuberculous mycobacterial infection, disseminated

fungal infection, Epstein-Barr virus infection (infectious mononucleosis), and malignant lymphoma—and that accurate diagnosis requires pathology investigations, including both microbiology and anatomic pathology. The family leaves the clinic, and the patient is lost to follow-up.

This scenario is played out daily in many countries across the world and illustrates one aspect of the crucial role that pathology has in ensuring effective health care, namely, diagnosis. Despite recent progress in controlling communicable disease, the need for pathology is growing as the burden of noncommunicable diseases increases. There were approximately 14 million new cases of cancer and 8.2 million cancer-related deaths in 2012 (Stewart and Wild 2014), but treating these cases accurately is impossible unless the pathological diagnosis is known. Cancer is predicted to increase by 70 percent by 2032, with more than 60 percent of these new cases in Asia, Central and South America, and Sub-Saharan Africa. Similarly, diagnosing and treating patients with diabetes mellitus—another developing epidemic in low- and middle-income countries (LMICs)—is impossible without the ability to measure the levels of glucose in the blood. The diagnosis and risk stratification of cardiovascular disease requires pathology, for example, to check levels of serum lipids such as cholesterol.

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This chapter specifies an essential minimal package of services that should be available in LMICs to provide access to pathology services that are of acceptable quality, affordable, and timely to a majority of the population, especially outside of major cities.

RANGE OF PATHOLOGY SERVICES

The term *pathology* means the *study of disease*. The knowledge gained from this study has led to development of the many diagnostic tests used in clinical practice. These tests are performed on body fluids, including blood, urine, sweat, saliva, and sputum; on tissue biopsies; and on cells obtained from needle-aspirated specimens.

The diagnostic role is a key aspect of what pathology laboratories do and is fundamental to the effective working of any health care system. An interview-based study of cardiologists and oncologists in Germany and the United States indicated that 66 percent of clinical decisions are based on results of in vitro diagnostic tests (Rohr and others 2016).

Pathology also supports clinical care by assessing disease severity and prognosis, for example, determining the staging and grading of a cancer by histopathology; this information is fundamental to deciding and managing treatment plans for patients. Equally important is the role of the pathology laboratory in monitoring clinical response to treatment, for example, analyzing blood levels of markers of renal function in patients with renal failure.

Pathology plays a number of other key roles. One is quality assurance within the health care system. In 2013, autopsies showed an estimated 20 percent major discrepancy between the pre-mortem clinical diagnosis and the autopsy diagnosis (Kuijpers and others 2014). Similarly, through the examination of surgical specimens, surgeons can learn whether they are fully excising tumors; through the use of microbiological culturing, physicians can correctly identify the cause of a fever. Pathology contributes to disease surveillance by helping identify new and emerging diseases such as the Zika virus; pathology facilitates the maintenance of disease registries that help inform national health policy and allocation of resources. Finally, forensic pathology is integral to legal systems around the world.

In all of these roles, pathology services encompass a number of disciplines and subspecialties; table 11.1 describes the main ones. In the United States and most other regions, these pathology disciplines are divided into two main groups:

- **Clinical pathology**, also called *laboratory medicine*, which is largely concerned with analysis of blood and

other fluids and involves, for instance, clinical biochemistry, microbiology, and hematology

- **Anatomic pathology**, which is concerned with cell and tissue analysis and involves cytology, histology, and autopsy.

In high-income countries (HICs), pathology services typically are provided in one of three ways:

- **Central laboratories that deliver most of their services in hospital settings.** Central laboratories have a common infrastructure that supports their various components, including specimen collection services, transport and reception, and a mechanism for transmitting the results of tests and accompanying reports to the ordering clinicians and patients. They have laboratory information systems (LIS) that are ideally connected to electronic patient records.
- **Smaller laboratories in more rural environments** that offer a more limited repertoire of tests, as well as point-of-care testing (POCT) in community settings.
- **A small number of laboratories, often in conjunction with university departments, that provide the most specialized tests.** These laboratories also undertake research, both in the field of pathology itself and with other disciplines as part of multidisciplinary teams. They also organize and provide education and training in pathology and related disciplines.

Although the core of laboratory activities may be considered the performance of tests and the analysis of the results (the analytical phase), it is important to recognize that the pre- and postanalytical phases are equally important for generating accurate laboratory test results (box 11.1). These phases range from the selection of the most appropriate tests or investigations to the interpretation of their results and the provision of clinical advice across the spectrum of medical specialties. In practice, this involvement may require a review of medical records and discussions with ordering clinicians. An example is the multidisciplinary meeting (tumor boards in the United States), in which pathologists, surgeons, and chemotherapy and radiation oncologists, radiologists, nurses, and others involved in cancer care of a patient meet to review all relevant information and decide on the best approach for treatment and management.

Pathologists may also provide leadership for hospital-wide quality assurance efforts. Increasingly, pathologists are assuming additional clinical roles in many health systems, for example, serving as infectious disease doctors, managing patients with metabolic disorders, and providing specialized oncology services.

Table 11.1 Major Pathology Disciplines and Roles

Clinical biochemistry	Study of the biochemical basis of disease
Cytopathology	Study of disease in individual cells
Forensic pathology	Determination of cause and manner of death for legal purposes
Hematology	Study of blood disorders
Histopathology ^a	Study of disease in human tissue
Immunopathology	Study of the immunologic basis of disease
Medical microbiology	Study of infection
Molecular pathology and genetics	Study of the molecular and genetic basis of diseases and heritable conditions
Pediatric and perinatal pathology	Study of the diseases of pregnancy, childbirth, and children
Transfusion medicine	Study of the collection, preparation, storage, and clinical use of blood products

Note: A selection of the major disciplines was derived, in part, from <https://www.rcpath.org>.

a. Histopathology includes a number of subdisciplines, such as dermatopathology, neuropathology, and others that focus on diseases of a single organ or organ system.

Box 11.1

Three Phases of Laboratory Testing

- **Preanalytical phase.** Selecting the appropriate test, obtaining the specimen, labeling it with the patient's name, providing timely transport to the laboratory, registering receipt in the laboratory, and processing before testing.
- **Analytical phase.** Performing the test and interpreting the result.
- **Postanalytical phase.** Preparing a report detailing the result and its interpretation, authorizing the report, and transmitting the report to the clinician so that the clinician can institute appropriate action.

In HICs, the largest proportion of errors in pathology occurs in the pre- and postanalytical phases (Plebani 2009). In the preanalytical phase, these errors include failing to ensure that the specimen is collected from the right patient, that the correct specimen type is collected, and that the specimen is collected at the right time. In the post-analytical phase, errors include reporting the wrong result and failing to read the report, making the wrong or no decision, or taking the wrong or no action.

Clearly, pathology is not a stand-alone service. Its value is as a crucial and integral part of the system of care in which the outcomes for patients and the operational and economic benefits for the system depend on all of the parts working effectively together. Without accurate diagnosis, everything else is compromised.

CHALLENGES TO PATHOLOGY SERVICES IN LMICs

The child described in the clinical vignette at the beginning of this chapter needed access to microbiology, hematology, and immunology services, and she almost certainly would have needed access to the expertise of a histopathologist. Yet access to diagnostic pathology services is not available in many countries and regions.

Ideally, the public sectors of LMICs should have three tiers of laboratories—with a small additional number of national or regional research or reference laboratories (WHO AFRO and U.S. CDC 2010). The tier 1 laboratories are widely distributed in the community and typically perform a small number of simple clinical pathology tests. Tier 2 and tier 3 laboratories are progressively fewer in number, provide tests of increasing complexity and capacity, and are found in progressively larger population centers. In many countries, however, especially poorer ones, such structures do not exist. Their absence has several causes, the most important of which is lack of human capacity, resulting in far too few trained personnel to staff the laboratories to provide adequate population coverage at all levels.

Inadequate Staffing

Data on staffing are lacking for much of the world, but the available data illustrate the problem. In Sub-Saharan Africa, at least five countries have no anatomic pathologist. Surveys of the other countries in the region have shown that the number of anatomic pathologists per patient population is approximately 1:1,000,000, or about one-fiftieth the ratio in the United Kingdom and the United States (Adesina and others 2013; African Strategies for Advancing Pathology Group Members 2015). In China, there were approximately 10,300 pathologists in all disciplines in 2015 (unpublished data from Chinese Society of Pathology 2015), constituting an estimated shortfall of 60,000–120,000. In 2014, there were only eight pathologists in a population of 14 million in Cambodia (Vathana and Stauch 2014); the ratio of pathologists per patient population in Vietnam was estimated to be 1:254,000 (Van Dang 2014). In upper-middle-income countries, the situation is somewhat better; for example, in Malaysia the ratio is 1:75,000 (Looi 2008).

Variable Standards

In addition to staff shortages, widely variable standards are an issue. Although the quality of services, particularly those provided in large cities in middle-income countries, can be good, frequently it is seriously inadequate in both urban and rural areas (Daramola and others 2016; Orem and others 2012).

A characteristic of many LMICs is that private laboratories—most staffed by pathologists from the public sector—are often run in parallel to the public sector and provide services to the population. The facilities in some of these laboratories can be as good as any internationally, but many are much less satisfactory. In India, where 70 percent of the laboratories are private, only 1 percent are accredited (Singh 2013). In Kampala, Uganda, which had more than 900 laboratories in 2011—96 percent of which were private—only 45 laboratories achieved the first step of the five-step process for international accreditation (Elbireer and others 2013).

The result of these challenges is that much of the population in LMICs does not have access to quality pathology services. As noncommunicable diseases that are particularly reliant on pathology for diagnosis and management become more prevalent, the level of misdiagnosis is likely to rise. This increase will result in unnecessary deaths and avoidable prolonged illness and distress, with attendant social disruption and negative impacts on productivity. The deficiencies also mean that data needed for disease surveillance and registries, and other types of population data needed to guide public policy and resource allocation, are not available. In addition, good quality pathology is necessary for the achievement of 11 of the 13 goals of the United Nation’s health-related Sustainable Development Goals (table 11.2); the deficiencies will impede attainment of these goals.

Table 11.2 Health-Related Sustainable Development Goals and Pathology

Sustainable Development Goals	Is pathology relevant?	Specific pathology examples
3.1: By 2030, reduce the global maternal mortality ratio to less than 70 per 100,000 live births	Yes	Testing for most common causes of maternal mortality, for example, infections; also blood transfusion for hemorrhage and autopsy to establish cause of death
3.2: By 2030, end preventable deaths of newborns and children under age five years, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-five mortality to at least as low as 25 per 1,000 live births	Yes	Testing and monitoring for most common causes of infant mortality, for example, infections, autopsy
3.3: By 2030, end the epidemics of HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases, and combat hepatitis, water-borne diseases, and other communicable diseases	Yes	Testing for communicable diseases, for example, blood tests for HIV/AIDS and malaria, antiretroviral resistance
3.4: By 2030, reduce by one-third premature mortality from noncommunicable diseases through prevention and treatment and promote mental health and well-being	Yes	Histo- and cytopathology for cancer diagnosis; hematology and biochemistry for diabetes diagnosis and management; pathology support for surveillance and other data platforms, for example, cancer registries
3.5: Strengthen the prevention and treatment of substance abuse	Yes	Toxicology tests
3.6: By 2020, halve the number of global deaths and injuries from road traffic accidents	Yes	Autopsy reports, blood banks for transfusion support

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Table 11.2 Health-Related Sustainable Development Goals and Pathology (continued)

Sustainable Development Goals	Is pathology relevant?	Specific pathology examples
3.7: By 2030, ensure universal access to sexual and reproductive health care services, including family planning, information, and education; and the integration of reproductive health into national strategies and programs	Yes	Blood and urine testing for pregnancy and for sexually transmitted diseases
3.8: Achieve universal health coverage, including financial risk protection; access to quality essential health care services; and access to safe, effective, quality, and affordable essential medicines and vaccines	No	—
3.9: By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals, and air, water, and soil pollution and contamination	Yes	Toxicology testing and diagnosis of related diseases
3a: Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries, as appropriate	Yes	Testing for smoking cessation in urine
3b: Support the research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect LMICs; provide access to affordable essential medicines and vaccines, in accordance with the Doha Declaration on the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement and Public Health	Yes	Pathology systems provide data, for example, surveillance, and research platforms
3c: Substantially increase health financing and the recruitment, development, training, and retention of the health workforce in LMICs, particularly in LICs and small island LMICs	No	—
3d: Strengthen the capacity of all countries, particularly LMICs, for early warning, risk reduction, and risk management of national and global health risks	Yes	Surveillance for emerging disease and through cancer registries

Note: HIV/AIDS = human immunodeficiency virus/acquired immune deficiency syndrome; LICs = low-income countries; LMICs = low- and middle-income countries; — = not applicable.

THE ESSENTIAL PATHOLOGY PACKAGE

The essential pathology package consists of a minimal suite of services that should be available in LMICs to provide access to pathology that is of reasonable quality, affordable, and timely to a majority of the population, especially that outside the main cities. The key concept is an integrated network of tiered laboratories (box 11.2, table 11.3), the tiers being similar to that described in the previous section. Thus, tier 1 is widely distributed in the community (both rural and urban). It has limited pathology capacity and staffing but can perform some basic tests and can refer patients and specimens to the next tier. The next tier has many fewer laboratories, probably located in sizable towns. It has greater capacity, performing most routine tests and when necessary, can refer more specialized tests to the to the next tier. These next-tier laboratories will probably be based in the largest towns and are capable of performing all routine tests and many specialized ones. Finally, depending on

the country and its pathology capacity, there may be a highly specialized laboratory performing complex testing that can act as a referral center for the country or even a region. These last two levels will often have educational and research capacity and be part of a university medical school.

This model is similar to the three-tier model in many LMICs (WHO AFRO and U.S. CDC 2010); the crucial aspect is that the model must be an integrated network of laboratories for more efficient and effective referral of patients across networks than would be the case with independent laboratories. This approach provides economies of scale, such as sharing use and costs of staff, equipment, and reagents. Other benefits include better communication, exchange of staff and knowledge, provision of education and training, and opportunities for research. This integrated approach would result in development of a critical mass of expertise and the optimal use of scarce resources.

Box 11.2

Definition of Laboratory Tiers

- *Tier 1.* Primary care and health center laboratories primarily serving outpatients in community settings, performing point-of-care tests and single-use tests, and referring more complex work to tier 2 or tier 3. These laboratories are staffed at the technician level.
- *Tier 2.* Laboratories in first-level hospitals that receive specimens from their own patients and receive referrals from tier 1 facilities. Usually, they have a pathologist and perform a selected number of routine tests.
- *Tier 3.* Laboratories in second-level hospitals that receive specimens from their own patients and receive referrals from tier 1 and 2 facilities. These laboratories have significant numbers of pathology staff and cover all routine testing in the major pathology disciplines.
- *Tier 4.* Laboratories in national or teaching hospitals that receive specimens from their own patients and receive referrals from tier 1, 2, and 3 facilities. They provide routine tests and highly specialized tests. In small countries, these facilities may be regional and shared by more than one country.

Each country and region has a different burden of disease and availability of staff, and some shifting of capacity may occur across the tier boundaries. For example, if a tier 2 pathologist makes regular visits, then fine needle aspiration cytology could be performed and reported in a tier 1 laboratory. In many countries, shortages of staff require that one laboratory fulfill the functions of both tier 3 and 4.

Table 11.3 Pathology Tiers

Laboratory features	Tier 1	Tier 2 (includes tier 1 capabilities)	Tier 3 (includes tier 2 capabilities)	Tier 4 (includes tier 3 capabilities)
Tests and test categories	POCT and single-use tests: malaria, tuberculosis, urinalysis, pregnancy, blood glucose, hemoglobin/hematocrit, ESR, blood typing Slide microscopy: malaria, wet preparation, stool parasites Preparation of FNAC and tissue specimens to send to tier 2 facilities	Many routine diagnostic and prognostic tests Clinical biochemistry urea and electrolytes, HBA1c for diabetes, liver, renal, bone, and lipid profiles Hematology complete blood counts, CD4 count, simple coagulation studies and thalassemia tests, support for whole blood transfusion Microbiology culture blood, urine, cerebrospinal fluid, sputum; simple antimicrobial susceptibility testing; serology for hepatitis A, B, or C and common infections	All routine and some specialized tests Clinical chemistry Endocrine tests: thyroid; cardiac markers, troponin, BNP; dynamic function tests, GTT; tumor markers: AFP, Ca-125, blood gases; therapeutic drug monitoring; serum and urine electrophoresis Microbiology Additional antimicrobial susceptibility testing, fungal cultures, mycobacterial cultures, viral load Hematology More advanced blood analysis, for example, component therapy, hemolysis, bone marrow studies, hematological malignancies, immunological studies	Specialized services as appropriate, surveillance, toxicology studies, support for transplantation, rare tumors, nutritional studies, support for clinical trials, mutational studies (cytogenetics, molecular analysis), gene analysis

table continues next page

Table 11.3 Pathology Tiers (continued)

Laboratory features	Tier 1	Tier 2 (includes tier 1 capabilities)	Tier 3 (includes tier 2 capabilities)	Tier 4 (includes tier 3 capabilities)
		Anatomic pathology FNAC, tissue biopsies and surgical excisions—processing, H&E stain and interpretation Hospital autopsy	Anatomic pathology Same as for tier 2, but with special stains including immunohistochemistry: ER, PR for breast cancer Specialized autopsy	
Staffing	Laboratory technicians supervised by general pathologist from distance	General pathologist, laboratory technicians, laboratory assistants; one of technicians manages laboratory	Mono-specialty pathologists, clinical scientists, specialized laboratory technicians, laboratory assistants, dedicated laboratory manager, possibly laboratory information systems coordinator, quality care manager Facilities and responsibilities for education and training of all levels of medical and nonmedical staff	Same as for tier 3 plus clinical trial specialists, data specialist Additional specialist educational capacity
Communication infrastructure	Paper or electronic, mobile	Paper or electronic or laboratory information system	Electronic or laboratory information system; telepathology (optional)	Same as tier 3 but more data linkages to trials and registries
Equipment	Simple microscope Rapid diagnostic tests POCT and single-use tests Specimen and patient identification FNAC and biopsy fixation	Automated blood and biochemistry analyzers; microbiology analyzers and incubators; blood typing including refrigerators; tissue processor and microtome for anatomic pathology	Automated tissue processor, equipment for full autopsy, immunohistochemistry station	Molecular biology and cytogenetics Immunofluorescence Electron microscopy for renal disease Possible biobanking for research
Turnaround time	Rapid, POCT, and single-use tests: 0–3 hours Send-outs, several days	An hour to several days	Routine: 1 hour to several days Complex: 7 days Autopsy: 30–60 days	Same as tier 3
Networks and surveillance	Accumulates and forwards incidence data to higher tier	Report to emerging disease, AST, cancer, and other NCD registries	Links to emerging disease, AST, cancer, and other NCD registries	Research on disease incidence trends, including AST and emerging diseases

Note: AFP = alpha-fetoprotein; AST = antimicrobial susceptibility testing; BNP = brain natriuretic peptide; Ca-125 = cancer antigen 125; ER and PR = receptor tests for breast cancer; ESR = erythrocyte sedimentation rate; FNAC = fine needle aspiration cytology; GTT = glucose tolerance test; H&E = hematoxylin and eosin stain (basic histopathology test); HBA1c = glycated hemoglobin test; NCD = noncommunicable disease; POCT = point-of-care tests.

Assumptions

1. Tiers may be adjusted as necessary to reflect the local burden of disease or local practice patterns and availability of trained staff.
2. Changes in technologies over time can shift tests and workloads across tiers.
3. Tests are examples (as applied to broad groups of infectious disease, cancer, and other NCD) and are not an exhaustive list.

In 2008, such national integrated laboratory systems were proposed as a key development for pathology services in Sub-Saharan Africa in the Maputo Declaration on Strengthening of Laboratory Systems (WHO AFRO 2008). Ethiopia was one of the first countries to successfully develop such a model; the

model was subsequently endorsed in the Freetown Declaration of 2015 (ASLM and WHO AFRO 2015) as the cornerstone of effective health care. Although infectious diseases were the focus of the original model, the principles are equally applicable to non-communicable diseases.

A key component in ensuring the sustainability of such a model is the tier 4 laboratory. These centers would offer specialized services as well as develop and provide research, education, and training, especially to the linked tier 1 and 2 facilities. Furthermore, these centers are most likely to develop innovations appropriate to the country's needs. Without these fostering and supporting roles, the long-term sustainability of the lower-tier laboratories will not be feasible. Linking such facilities to other centers of excellence (North-South, South-South) to provide access to further expertise and resources is important for continuing long-term development.

The model outlined in box 11.2 is intended to represent the minimum that a lower-middle-income country would provide. Countries at higher levels of development can build on this model to deliver increased provision appropriate to their needs. Conversely, the model serves as a goal for LICs to achieve as resources become available and are invested.

To ensure this network is sustainable, effective, and of good quality, five components are vital:

- Leadership
- Education, training, and continuing professional development
- Emerging technologies
- Quality management and accreditation
- Reimbursement policies for pathology services.

Leadership

The effective and efficient operation of a pathology laboratory is a multidisciplinary effort. Pathology services are primarily delivered by three groups of professionally qualified staff—pathologists, clinical scientists, and technicians (also referred to as *technologists*)—supported by assistants, managers and administrators, and technology specialists. In most places, clinical scientists or technicians undertake the role of administrator or manager. Pathologists provide leadership and serve as the interface between laboratory and clinical services; in some countries and specialties, pathologists share these roles with clinical scientists. Pathologists and clinical scientists also oversee quality improvement and service development as well as pathology-led research and development. Laboratory technologists are responsible for delivering the technical aspects of the service.

The goal of this joint effort is to provide a service that is patient oriented and meets clinical needs. These clinical needs are defined by standards of care, expectations of individual physicians, and patients. Accordingly, laboratory leadership needs to monitor the activities of staff to ensure that clinically relevant services are being provided.

This administrative oversight is a key leadership responsibility required by International Organization for Standardization (ISO) 15189:2012, the international reference document for best laboratory practice (ISO 2012).

Laboratories produce information that result from their processes, personnel, and equipment. This information is also influenced by the clinical settings in which the laboratories operate and from which they receive specimens. Patient-specific, disease-specific, and therapy-specific factors may influence the information that the laboratories produce. Those in leadership positions need to understand the interactions between these factors, especially as those interactions affect how the information will be used for patient care. The Joint Commission International's accreditation standards for hospitals state that for the purpose of clinical consultation and rendering of medical opinion, the laboratory should be led by physicians, preferably pathologists (JCI 2014). Pathologists, as clinicians, have insights into the thought processes behind requests for laboratory tests and the decisions that may be made with the information received. These insights are not only invaluable in determining how to most effectively organize and direct laboratory services, but they are also crucial to provision of clinical advice on the further investigation and management of individual patients. Clinical scientists, who have had training significantly similar to that received by clinical pathologists, may also provide this level of leadership.

Reflecting the integral role that pathology plays in the wider health care system, laboratory leadership also needs to be involved in the development of national strategic plans for laboratories. These plans detail the long-term vision and mission of the nation's laboratory services. To be effective, development of this national blueprint needs to recognize the local disease burden, available clinical skills and services, clinical requirements for diagnosis and monitoring, and technical realities. The primary involvement of clinical laboratory leadership, in conjunction with other clinicians, is to provide guidance for the definition of policy that delineates the organization, scope, and nature of the laboratory service according to the tiers providing health care in the respective countries (WHO AFRO and U.S. CDC 2010).

Pathologists provide leadership at the operational level. Doing so entails the ability to read about and understand scientific and technological advances in the field of medicine as well as improvements in laboratory technology. Changing clinical demands for patient care, as documented in new and revised versions of locally applicable clinical care guidelines, require a laboratory director's involvement and informed response. Similarly, advances in the technical capacity of laboratories, including the introduction of new tests and the withdrawal of obsolete ones,

need to be assessed in relation to their ability to improve the clinical effectiveness of the laboratory, as well as the clinical effectiveness and cost-effectiveness of the whole care pathway. To effectively lead the response to such changes, pathologists need the authority to alter aspects of the operations to ensure that laboratories remain true to their goal of enhancing the quality of patient care.

Education, Training, and Continuing Professional Development

Educating and training larger numbers of qualified personnel is clearly of paramount importance in developing a sustainable pathology network. There are three major categories of staff: pathologists, clinical scientists and technologists, and technicians. Their education consists largely of a combination of formal courses for degrees and diplomas and hands-on training and experience under the supervision of qualified individuals.

Pathologists

Historically, pathologists in LMICs were educated in Australia, Europe, and North America; the individuals often resided in the HICs for the duration of their training programs. Although those funded by governments or charities were expected or required to return home when the training was completed, large numbers stayed in HICs. In contrast, clinical scientists and technicians predominantly received their education locally.

Pathologists are medically qualified practitioners who have undergone postgraduate education and training in pathology. There are three main models of training; the first two are common in LMICs:

- In the first training model, pathologists are trained as generalists dealing with all aspects of pathology, both clinical and anatomic; this is also called *general pathology*. This postgraduate training period is usually two to four years. In some countries, the course entails a university degree.
- In the second model, pathologists are trained only as either clinical or anatomic pathologists. The postgraduate training period is two to three years.
- In the third model, pathologists are trained as mono-specialists, for example, as hematologists, microbiologists, or clinical biochemists. Such individuals tend to be employed in academic centers. This model reflects countries with more-developed health care systems, such as South Africa. The postgraduate training period is usually a minimum of four years. In much of South America, pathologists are only trained as mono-specialty anatomic pathologists; the other disciplines of pathology are staffed by clinical scientists, such as clinical biochemists.

These training courses are largely experiential in nature, with considerable hands-on involvement in pathology service delivery supplemented by small group teaching and formal lectures.

Clinical Scientists and Technologists

In some countries, clinical scientists perform functions similar to those of pathologists. They follow a similar pathway of education and training to achieve the required competence, for example, in clinical biochemistry, immunology, microbiology, or virology. Clinical scientists may also be responsible for the performance of specialized services, such as molecular genetics, toxicology investigations, and electron microscopy. These individuals generally have degrees in chemistry, biological science, or biomedical science, usually followed by a master's or doctoral degree in such areas as microbiology or clinical biochemistry. The training period is four to eight years. There may be subsequent subspecialization in such fields as virology.

Technologists are also sometimes referred to as *medical laboratory scientists* or *biomedical scientists*. Their education and training in some places involves the acquisition of a university degree, while in others it is similar to that of technicians.

Technicians

Technical staff are usually educated and trained through college courses, often part-time over several years. The education may encompass all of the specialties of pathology or it may be restricted to one of the major specialties, such as anatomic pathology or microbiology; such specialization is a feature of more developed laboratory services. In some countries, technical staff do not have formal qualifications and only receive hands-on training in the laboratory.

In most countries, in addition to the professional qualification or appropriate university degree, individuals need to be registered with the national registration body as an indication of required competence before being allowed to practice.

LMICs have increasingly developed their own pathologist postgraduate educational and training systems. In Sub-Saharan Africa, 21 countries have developed training programs in the past 25 years. In the 14 countries for which comparative data are available, the number of pathologists increased from 70 in 1990 to 370 in 2015 (Nelson and others 2016). Similarly, in Malaysia, the number of pathologists increased from approximately 50 in the 1980s (Jegathesan and de Witt 1982) to more than 500 in 2016 (Looi 2008).

However, in many countries, especially low-income countries (LICs), the shortage is such that training

enough pathologists to fully staff all relevant sections of health care systems is not possible, even in the medium term. Accordingly, the expansion of the training of scientists and technicians and the exploration of task-shifting and task-sharing are needed, with parallel development of shorter training programs focused on specific tasks, such as cytology screening.

A program of continuing professional development (CPD) is necessary to maintain the standards and long-term sustainability of the pathology network. Many individuals and institutions provide CPD events, often delivered by visiting individuals and organizations, on an informal basis; systematic institutional and national programs are rare in LMICs. One of the most common support requests from pathologists in LMICs is for provision of and access to CPD. Without such programs, the knowledge and skills of individuals can become out of date, especially as the pace of advances accelerates.

Emerging Technologies

Diagnostics

In all health care systems, the need for medical tests at any point in the care pathway requires that specimens be collected and sent to laboratories for analysis and interpretation. Laboratory testing can be centralized, provided at the point of care, or more typically a combination of the two. The selection of which approach to take is partly driven by the availability of a given test at the point of care, the level of test volumes, and the need to have test results available at the time of the patient

encounter. These considerations need to be balanced against the generally higher cost of providing POCT, albeit resulting in savings elsewhere in the care pathway, and the technical challenges of generating accurate test results at that level.

A tiered system of laboratory testing that focuses on the type of care provided within each tier, as well as the number of tests performed within each tier, can be used to design approaches to testing. For example, tier 1 facilities would most benefit from POCT; tier 3 facilities would benefit most from centralized laboratory testing. Test devices used for disease surveillance purposes can be designed for centralized use only.

Device manufacturers and public-private partnerships have developed new technologies for laboratory testing to provide both POCT and centralized testing within a tiered system of health care delivery, increase and improve access to laboratory testing in general, and bring new diagnostic tests to the public. Key challenges for the development and use of emerging tests are shown in box 11.3. In particular, simplicity of specimen collection, device use, and interpretation and communication of test results are critically important because new devices will be used in many LMICs by persons with widely varying languages, backgrounds, training, and expertise.

Many of today's laboratory analyzers require a reliable external power supply, and because electricity supply can be intermittent in many LMICs, even with back-up facilities such as diesel generators, there is increasing focus on developing devices that require no

Box 11.3

Effectiveness Criteria for Emerging Tests

- Any new tests should provide results for a specified clinical problem to guide clinical decisions, for monitoring disease status or response to therapy, or for data collection for disease surveillance.
- Results of tests designed to be used in clinical care should be available in a time frame that will guide clinical decision making.
- Tests should be easy to perform, and results must be easy to interpret and communicate.
- Target performance characteristics—such as sensitivity, specificity, predictive values, precision, and accuracy—for the intended uses should be specified before test development.
- Manufacturers' claims regarding test performance characteristics should be independently verified.
- Test platforms should be usable and stable in locations of intended use.
- Test platforms should meet procurement requirements for supply chain, maintenance, availability of quality control standards, durability, and stability in variable climatic conditions.
- Test costs should be affordable in locations of intended use.

Source: Based on Wu and Zaman 2012.

power or have built-in power generation (Pollock and others 2013; Whitesides and Wilding 2012; Yetisen, Akram, and Lowe 2013). In addition, because of the challenges of supply chains and storage in many LMICs, interest is growing in developing POCT devices that require minimal or no reagents other than the devices and that can be stored for long periods in hot and humid climates with no performance degradation. For larger analyzers used in central laboratories, one goal is to develop test platforms that can support a number of different assays rather than platforms that are unique to one set of tests. The development of flexible platforms would minimize the number of devices needed, with associated reductions in acquisition and maintenance costs; it would also allow for rapid introduction of new assays, a particularly important consideration in light of emerging diseases in LMICs.

Molecular diagnostic techniques have historically been substantially more expensive and required technical expertise and laboratory infrastructure unavailable in most LMICs. This field of diagnostics is rapidly evolving to the point where some tests are becoming practicable for use in LMICs (St. John and Price 2014), and this trend is likely to accelerate. Access to these tests is becoming a routine part of health care delivery because a number of diseases and conditions are only detectable using these methods. For example, many cancers are now classified using molecular tests, and the use of some drugs requires molecular testing to determine whether specific biomarkers are present.

Point-of-Care Testing

POCT is usually performed by medical staff, nurses, or medical assistants using small, mobile testing devices. It can be used anywhere on the care pathway—first-level, second-level, or third-level care—as well as in patients' homes. This approach differs from centralized laboratory testing, which is performed by specialized technicians using large-capacity (high-throughput) analyzers.

Although POCT technologies are broadly based on the same techniques used in centralized laboratory analyzers, they have reduced reagent and sample volume requirements, rely upon stabilization of reagents, and typically use single-use cassettes for testing.

In LMICs, POCT has been used extensively to help guide the treatment of several diseases and conditions. Expanded access to POCT is cost-effective in extending life expectancy in patients with HIV/AIDS (Cassim and others 2014; Hyle and others 2014; Wu and Zaman 2012). Access to smear microscopy, rapid malaria diagnostic testing, or both has played an important role in decreasing malaria-related morbidity and mortality (WHO 2015b). Access to rapid detection of infection

and limited antimicrobial susceptibility testing for tuberculosis has significantly enhanced global efforts in diagnosis and treatment (WHO 2015a).

However, the use of small specimen volumes causes substantial challenges in the design of systems that can yield consistent test results (Bond and Richards-Kortum 2015). As a result, POCT may not produce test results that agree with those generated by larger laboratory analyzers. The results from POCTs need to be harmonized with those from a central laboratory analyzer so that health care providers are familiar with any variations in the results.

Data Handling

Clinical laboratories generate large volumes of data for patient care as well as for quality control and other laboratory-management operations. As access to laboratory services increases in LMICs, paper reporting systems will not support the high volumes of data. An integrated, tier-based laboratory system requires the ability to transmit data to and from multiple testing sites as well as to forward results to clinicians and selected test results to patients for self-monitoring, to public health authorities, and to disease registries. These data-handling needs will only be achieved by the use of LIS (NPP 2014). Although many commercial systems are not affordable in LMICs, open-source systems are available that may provide opportunities for local use. Development of robust, reliable LIS that can be integrated with other parts of health care data systems needs to be a priority in all regions. Mobile phones may facilitate the process.

Part of the data used in diagnostic testing consists of images, including for surgical pathology (histopathology) and cytopathology, hematology (blood smear examinations), microbiology (identification of parasites based on morphologic examination), microscopic examination of urine specimens, and malaria smears. One approach to diagnostic testing, consultation, and quality control is the use of telepathology—the transmission of images via Internet connections to and from remote sites. Previously, this technology was expensive and required access to bandwidth not available in most of the world. More recently, costs have decreased, and improved Internet connectivity is available in many regions.

Quality Management and Accreditation

Although access to quality pathology laboratory testing is an essential part of modern medical practice, in some settings most laboratories are not accredited and do not meet minimal standards for good laboratory practice. These laboratories are unlikely to consistently generate accurate or reliable test results. The absence of accurate

and reliable results can lead to incorrect diagnoses, inappropriate treatment, wasted resources, and even lost lives. Such situations give credence to the saying that “no test is better than a bad test.”

Causes of Suboptimal Testing

Laboratory testing is a complex process with preanalytical, analytical, and postanalytical phase variables (box 11.1). Considering analytical influences alone, test methodologies affect the magnitude of false positive and false negative results. Sensitivity and specificity profiles influence choices for screening and confirmatory tests. The competence of personnel, regular quality control, state of equipment and laboratory infrastructure, and access to reagents affect the accuracy of test results. A lapse in any step in the long chain of processes can result in incorrect and potentially harmful test results. Ethics and accountability are as important in laboratories as in any other component of health care.

Quality Management

To control these variables, it is essential that laboratories make the commitment to a quality management system and organization structure that ensures that tests are fit-for-purpose, standard operating procedures are documented and followed, personnel are suitably qualified and trained, and regular audits are conducted. The practice of interlaboratory comparisons, such as external quality assurance (EQA) and proficiency testing (PT) programs, has evolved to encourage laboratories to meet validated performance benchmarks. Many comprehensive EQA and PT programs are available regionally and globally (box 11.4). These programs vary in strength; some are educational, while others have a validation focus.

Audit practices have extended beyond internal activities to assessments by third parties using national and international peer-determined standards. The formal assessment of laboratories by independent external agencies against such standards, known as *accreditation*, is the norm in HICs, where requirements for laboratory practices are often mandated by law. Apart from ensuring quality, accreditation status affects the profitability and marketability of laboratories; only accredited tests are reimbursed by health insurance. Through mutual recognition agreements, such as the Asia-Pacific Laboratory Accreditation Cooperation, the Inter-American Accreditation Cooperation, and the International Laboratory Accreditation Cooperation, the tests performed by accredited laboratories are recognized by signatories across country boundaries.

In LMICs, the culture of interlaboratory comparison, audit, and accreditation has yet to become firmly established. In India, it is estimated that fewer than 1 percent of the approximately 100,000 pathology laboratories are accredited (Singh 2013). A 2013 survey reported that more than 90 percent of countries in Sub-Saharan Africa had no laboratories accredited to international quality standards; of the laboratories that were accredited, more than 90 percent were in South Africa (Schroeder and Amukele 2014). Laboratory accreditation has not been established in many LMICs in Southeast Asia, partly because most LMICs do not have national health insurance plans, and the incentive of reimbursement for tests conducted by accredited laboratories does not apply. In addition, most LMICs lack strong regulatory oversight of laboratory practice. Laboratory tests performed by public laboratories, which are frequently resource constrained, are heavily subsidized by governments,

Box 11.4

Examples of External Quality Assessment Programs

International Programs

- Royal College of Pathologists of Australasia Quality Assurance Programs, Australia
- National External Quality Assessment Services, United Kingdom
- College of American Pathologists, United States
- Randox International Quality Assessment Scheme, international
- International Academy of Pathology, international with regional and national divisions.

National and Local Programs

- Bureau of Laboratory Quality Standards, Thailand
- External Quality Assessment schemes of Faculty of Medical Technology, Mahidol University, Thailand
- Laboratory Quality Assurance Scheme, Malaysia
- National Center for Clinical Laboratories, China
- Indian Association of Medical Microbiologists, India
- National Health Laboratory Service, South Africa (this program extends to other Sub-Saharan African countries).

while private laboratories benefit from out-of-pocket payments. EQA and PT are not mandatory. The situation pits profit against quality, and many LMICs struggle with the mushrooming of corner shop–type private laboratories with substandard practices and questionable accountability.

However, practices in many emerging economies are rapidly changing, and laboratory accreditation is now actively sought. Although most laboratories started by seeking accreditation from foreign agencies (for example, Australia’s National Association of Testing Agencies and the College of American Pathologists), this approach has proved unsustainable because of the high expense. Today, government-backed national accreditation agencies adopting international standards, especially ISO 15189 for medical testing laboratories, provide assessments at a more reasonable cost. Examples of accreditation agencies are listed in box 11.5.

However, legislation-backed regulation of laboratories in LMICs remains the exception (Looi 2008; Wattanasri, Manorama, and Viriyayudhagorn 2010), and participation in EQA or PT programs and accreditation is entirely voluntary. For these emerging economies, the impetus to gain accreditation has been competition and market driven, especially in light of trade agreements such as the ASEAN (Association of Southeast Asian Nations) Free Trade Area, the World Trade Organization, and the imminent Trans-Pacific Partnership Agreement.

In Sub-Saharan Africa, because public laboratories are the main providers of services, the WHO Regional Office for Africa in 2009 introduced the Stepwise

Laboratory Improvement Process Towards Accreditation checklist and the Strengthening Laboratory Management Toward Accreditation training curriculum. These programs were jointly developed with the U.S. Centers for Disease Control and Prevention, the Clinton Health Access Initiative, and the American Society for Clinical Pathology to assist laboratories to move toward accreditation status (Gershy-Damet and others 2010). Although much remains to be done, these tools have transformed the laboratory mindset and practice landscape in Sub-Saharan Africa (Alemnji and others 2014; Yao and others 2014).

The cooperation of the WHO, governments, and national professional bodies has been crucial in the global paradigm shift in laboratory testing to quality and international standardization. However, many challenges remain for LMICs; the most important are resource constraints; establishment of national EQA, PT, and accreditation programs; and legislation-backed regulation of laboratories. Ensuring the long-term, good quality of the services provided by the essential pathology package requires the adoption of an appropriate form of accreditation, within which EQA is embedded.

Reimbursement Policies for Pathology Services

Pathology tests are almost universally costed according to the complexity and the volume of tests performed, often referred to as the *cost-per-test* or *activity-based costing*. Who pays for the tests varies and is closely related to overall health reimbursement policies.

Box 11.5

Examples of Accreditation Bodies

- College of American Pathologists, Laboratory Accreditation Program, United States
- Joint Commission International, United States
- National Association of Testing Authorities, Australia
- South African National Accreditation System, South Africa
- United Kingdom Accreditation Service, United Kingdom
- International Accreditation New Zealand, New Zealand
- Comité Français d’Accréditation, France
- Standards Council of Canada, Canada
- China National Accreditation Service for Conformity Assessment, China
- Hong Kong Accreditation Service, Hong Kong SAR, China
- National Accreditation Board for Testing and Calibration Laboratories, India
- Bureau of Laboratory Quality Standards, Thailand
- Medical Technology Council, Thailand
- Department of Standards Malaysia, Malaysia
- General Coordination for Accreditation, Brazil
- Bureau of Accreditation, Vietnam
- Komite Akreditasi Nasional, Indonesia.

China has a complex reimbursement system for pathology services. The national health care system accounts for the majority of medical reimbursement, but individual provinces and cities have their own differing reimbursement policies. This variation is reflected in the big gap in health care benefits between wealthy and poor regions in China (Chen, Zhao, and Si 2014; Pan and others 2016). In Tianjin, a large city with a population in excess of 13 million people, the health care policy states that public medical insurance covers approximately 70 percent of laboratory testing provided in local hospitals. The remaining laboratory tests are paid on an out-of-pocket basis. In practice, however, the government usually only reimburses basic laboratory tests; because complex tests carry high price tags, only 40 percent of the actual cost of pathology testing is covered (Lei, Chen, and Lu 2014; Mao 2012; Pan and others 2014). In addition, the circumstances under which pathology tests can be used are restricted. The result is that most of the burden of the costs of laboratory tests falls on patients. In some rural areas, especially the more rural regions of western China, coverage of medical costs, including pathology services, is even less generous.

In India—with more than 40,000 hospitals and 100,000 diagnostic laboratories—the private sector delivers 70 percent of health care, including laboratory services. Public financing for health care is less than 1 percent of gross domestic product; only 17 percent of the population is covered by any kind of health insurance. Accordingly, more than 70 percent of health expenditures, including for pathology services, is borne by families as out-of-pocket payments (*The Hindu* 2014).

In Sub-Saharan Africa, the picture is mixed. In South Africa 80 percent of the population has health care, including pathology, paid for by the government. Patients only make a payment if they can afford to. About 7 percent have personal insurance, while the remainder pay out of pocket. A similar situation exists in Zimbabwe and Botswana. In East Africa, there is a mixture of government, insurance, and self-payment. In other

countries, self-payment is more common. Payment for testing is made in advance, with patients and families purchasing the necessary supplies to perform the tests in addition to paying the fee required for testing.

Some LMICs have community-based health insurance programs that households can join, but the coverage provided varies. Ghana's program covers only hospital-based services. In Bangladesh, nongovernmental organizations operate insurance programs and cover services in their own clinics. Whether laboratory tests are covered in these programs depends on the details of the particular programs (Robyn, Sauerborn, and Bärnighausen 2013; Soors and others 2010; Wang 2012).

The key factor that applies to all programs is that both patients and clinicians worldwide have a tendency to prefer to use their limited financial resources for treatment rather than diagnosis. If payment is out of pocket, the tendency is for fewer, less complex, and lower-quality tests; the opposite is the case when reimbursement is provided by national or private programs. Invariably, this bias reduces the eventual quality of the outcome. Moreover, it adversely affects the ability of health care systems and governments to standardize health care delivery, collect epidemiological data, and assess the effectiveness of policies and interventions.

To optimize the benefits of pathology provision, as little as possible of the costs should be on an out-of-pocket basis. Where countries adopt a model of universal health coverage, we propose that pathology reimbursement be an integral component of the reimbursement system. Clearly, it will be important to ensure that in such a model, pathology costs are kept in check, for example, by the institution of guidelines on the use of tests.

Economics of Pathology in Different Countries

This section analyzes the costs of pathology laboratories using data from countries with different income levels and with varied health systems (table 11.4). These analyses provide some interesting insights, although data are

Table 11.4 Approximate Annual Salary of Pathology Staff, by Country Income Category, 2010 U.S. Dollars

WHO employee category and corresponding pathology staff	Low-income country	Lower-middle-income country
2: laboratory assistant (secondary education or diploma)	2,220	4,800
3: laboratory technician (bachelor's degree)	2,870	6,170
4: scientific officer (master's degree)	4,550	9,800
Pathologist (physician with additional training)	13,650	29,400

Source: Based on ongoing estimates from Serje 2015.

Note: WHO = World Health Organization. The WHO data are from International Labour Organization salary databases. Equivalencies for technicians, and construction of the top category at three times the salary of category 4 by authors, also is based on unpublished data for Tata Memorial Hospital, Mumbai, as a guideline.

limited and not always readily comparable. These variations on unit costs of tests help explain why estimating the costs of an essential pathology package is challenging.

Pathology’s Share of Health Costs

One study for the United States suggested that laboratory tests account for 4.5 percent to 10 percent of total health expenditures (Avivar 2012), compared with 5 percent for Spain (Avivar 2012), 3.3 percent for the United Kingdom (Department of Health, United Kingdom 2006), and 3 percent for Australia (CIE 2016). The payment system in the United States, in which doctors receive payment on a per test basis (and are particularly conscious of potential litigation) means that the United States is likely to be an outlier among HICs. In South Africa, the costs of pathology are about 3.5 percent of total health care expenditure (Pillay 2012). We have no data on the share of pathology costs in overall health expenditure in other LMICs.

Cost per Laboratory Test

Cost per laboratory test undertaken varies considerably. Important factors include the type of test (the diagnostic area), the volume of tests undertaken in the laboratory (the scale), the level of national income and salaries of technical personnel, whether the test is undertaken in the normal workflow or on an urgent or rapid-turnaround basis, and a hard-to-measure efficiency factor. Since the level of the laboratory (tiers 1 through 4) affects the mix of tests undertaken, the cost per test also varies with the level of the laboratory.

Some diagnostic areas are more standardized and more automated than others. Data from the United Kingdom (Department of Health, United Kingdom 2008) found that the median direct cost—excluding equipment costs, costs of space, and overhead costs—of a specific routine test in biochemistry across a sample of laboratories was £1.00 compared with £2.40 in hematology, £6.90 in microbiology, and £48.10 in histopathology (2006/07 costs) (the corresponding costs in 2012 U.S. dollars are US\$1.94, US\$9.03, US\$13.39, and US\$93.31). In some disciplines, it has been possible to use equipment, such as large analyzers, to lower the costs per test. In these areas, staff costs are a smaller proportion of the test cost (68 percent to 87 percent for biochemistry tests across different sites and 74 percent to 89 percent for hematology, with one outlier). In other disciplines in which automation is not as extensive, the unit costs are higher, and staff costs are a higher proportion of test costs at 72 percent to 92 percent for microbiology and 93 percent to 97 percent for histopathology (Department of Health, United Kingdom 2008). As science and technology progress, areas such as microbiology may become more automated and less costly; however, newer and less automated tests will continue to be developed.

There are strong economies of scale in laboratory testing (for example, Department of Health, United Kingdom 2008; Cunnamana and others 2016 for tuberculosis tests in South Africa). However, the tradeoff is that increased centralization of tests is also associated with increased turnaround time and potential loss of patients to follow-up. In table 11.5 the smallest laboratory performs

Table 11.5 Estimated Ingredients for General Pathology Laboratories at Different Levels, Lower-Middle-Income Countries

Assumptions	Tier 1 laboratory	Tier 2 laboratory	Tier 3 laboratory
Facility description	5 health workers; no inpatients	100 beds	200–400 beds
		5 surgeries per day	15–20 surgeries per day
		500 outpatients per week	1,500 outpatients per week
Population served	30,000	50,000–200,000	3 million to 6 million
Approximate annual hospital budget	US\$150,000	US\$6 million	US\$18 million
Laboratory staff, excluding administrative support	1 laboratory technician	1 general pathologist	4 pathologists
		4 laboratory technicians	2 clinical scientists
		2 laboratory assistants	12 laboratory technicians
			8 laboratory assistants
			1 medical officer
Laboratory test volume per week	100 malaria slides plus point-of-care tests	850	2,500

table continues next page

Table 11.5 Estimated Ingredients for General Pathology Laboratories at Different Levels, Lower-Middle-Income Countries (continued)

Assumptions	Tier 1 laboratory	Tier 2 laboratory	Tier 3 laboratory
Equipment needs	US\$2,000–US\$5,000 (microscope; small devices)	US\$150,000–US\$200,000	Varies according to functions
Annual salary cost, (using table 11.4)	US\$4,800	US\$63,680	US\$259,440
Overall annual laboratory budget, assuming consumables: salaries are 4:1 in hospitals	n.a.	US\$318,400 (5.3 percent of hospital budget)	US\$1.3 million (7.2 percent of hospital budget)

Sources: Based on economic ratios from table 11.6, salaries from table 11.4, and expert judgment. Published data were for hospitals; insufficient data were available to make complete estimates for a tier 1 facility.

Note: n.a. = not applicable.

about one test per employee per day, compared with 24 in the medium-sized laboratory in India, and 43 billable tests in the largest laboratory in the United States. We used 300 days worked per person per year as a rough guide for this calculation. No data on staff were available for Thailand.

The level of national income affects the technology used in conducting tests, and hence the relative shares of different cost components. In LMICs, salary costs are lower relative to the cost of reagents and test kits, so tests tend to be less automated; however, staff costs form a smaller proportion of overall costs. In HICs, salary costs are higher relative to the cost of consumables, and there is more automation; but salary costs form a higher proportion of overall costs (see table 11.6; some caution in interpretation is needed because the four laboratories in the table do not serve identical functions). In the United States, the ratio of staff to consumables in total costs has increased. The ratio was 40:60 in 1980 for one clinical biochemistry laboratory in a university hospital, but rose to 60:40 by 1990 (Benge, Csako, and Parl 1993). It is likely that LMICs will follow a similar trend as salaries increase and drive increased automation.

Estimated Costs for the Essential Pathology Package

Although the variations in the unit costs of tests make estimating laboratory costs challenging, systematic factors are involved as well. We first estimate salary costs for technical staff using the WHO-CHOICE data (table 11.4) for the average LMIC. We then construct stylized laboratories using expert judgment combined with published data summarized in table 11.6. We combine these stylized data with the salary data and with the estimate that consumables in the laboratory cost approximately four times as much as salaries in Asia (which is slightly lower than the

ratio for the two big hospital laboratories in India and Thailand, summarized in table 11.6). In Sub-Saharan Africa, the current ratio is closer to 1:1 (Kuti, personal communication); this ratio is likely not to be optimal given that too few tests are undertaken in Sub-Saharan Africa.

These inputs yield estimates of recurrent laboratory costs as a proportion of hospital budget of slightly more than 5 percent for a first-level hospital, and slightly more than 7 percent for a second-level hospital. Our estimates can be compared with data for Ghana, where the share of laboratories in total hospital costs was 2.3 percent for a first-level hospital with 117 beds and one doctor, and 4.1 percent for a second-level hospital with 100 beds and three doctors (Aboagye, Degboe, and Obuobi 2010). In India, the corresponding shares were 7.3 percent for a first-level hospital of 400 beds and 24 doctors, and 9.2 percent for a second-level hospital of 778 beds and 237 doctors (Chatterjee, Levin, and Laxminarayanan 2013).

We do not have enough data to estimate laboratory costs for primary health centers. One study of 12 government primary health centers in Ghana (Dalaba and others 2013) estimated that the costs of laboratory supplies amounted to less than 1 percent of the overall cost of the center. This figure excludes the cost of consumables for POCT that do not enter the laboratory.

Because of too little published data, our confidence that these numbers apply in LICs is low. Professional salaries in LICs are about half the level of those in lower-middle-income countries (table 11.4). However, it is unlikely that the costs of laboratories would be half as well. The volume of tests is likely to be lower, and unit costs are likely to be higher by an unknown amount. The data from Malawi (Gopal, personal communication) show that salaries of laboratory personnel are closer to the levels of lower-middle-income countries than the

Table 11.6 Structure and Annual Cost of Tier 3 and 4 Laboratories in Four Settings

	Lilongwe, Malawi	Tata Memorial Hospital, India Hemopathology lab	King Chulalongkorn Memorial Hospital, Thailand	Major teaching hospital, United States
Types of test	91% histology, 9% cytology	Primarily hematological malignancies	85% biochemistry; 15% hematology	Full service
Staff	2 pathologists 2 laboratory technicians 1 laboratory assistant	2 physicians 2 senior residents 6 scientists (2 PhDs) 2 technical officers (MSc) 13 technicians (BSc) 6 assistants Total 31	n.a.	7 pathologists 7 technical supervisors 19 phlebotomists 4 blood banks 18 molecular and microbiology labs 26 clinical biochemistry and hematology labs 11 processors 25 outpatient laboratory technicians 117 total, excluding administration
Approximate population coverage	1 of only 2 such laboratories, country of 15 million	City of 21 million, state of 112 million, diagnostic center for region	City of 6.3 million	City of 650,000 State of 5.3 million
Annual number of tests	1,680	227,000	2.16 million	1.5 million billable (7 million total)
Annual budget US\$ (year)	243,000 (2012)	976,270 (2012)	25.3 million in 2002 (\$ 2012)	18 million (2015) (2.7% of hospital budget)
Budget shares (%)				— ^c
• Space, utilities	n.a.	2.8	1.9 (equipment + space)	
• Equipment	22.6	11.2	13.2	
• Staff	61.7	13.9	84.9	
• Consumables	14.4	71.1	0	
• Miscellaneous	1.2 ^a	1.1 ^b	n.a.	

Sources: Gopal (personal communication) and Gopal and others 2013; Gujral and others 2010 for India; budget shares calculated by chapter author from published data; Charuruks, Chamnanpai, and Seubling 2004 for Thailand.

Note: n.a. = not available.

a. Communications costs, telepathology link with University of North Carolina.

b. Quality control, usually additional tests.

c. Data (Christopher Price, personal communication) from a hospital trust in the United Kingdom suggest that the split is 72 percent staff, 26 percent equipment rental, 1 percent equipment maintenance, and 1 percent other.

WHO data predict, likely because technically qualified staff are sufficiently scarce that if they were paid less, they would not remain in public laboratories in LICs.

In summary, our rough estimates (table 11.5) are that recurrent laboratory costs for a first-level hospital should be slightly more than 5 percent of the hospital budget; for a second- or third-level hospital, they should be slightly more than 7 percent of the budget. Of this share, about 16 percent consists of staff costs, and the balance consists of consumables. Costs for a tier 1 laboratory are

more modest, but most of the testing at this level is point of care, and we do not have data on the cost of POCT. What is known from HICs is that POCT is generally more expensive on a cost-per-test basis compared with centralized testing, primarily because POCT is based on single-use technology.

The cost of setting up a laboratory is estimated to be US\$2,000–US\$5,000 for a tier 1 laboratory; US\$150,000–US\$200,000 for a tier 2 laboratory at a second-level hospital; and a considerably larger amount at a third-level

hospital, but no estimates were made because of the wide variety of equipment choices available. In comparison, the equipment for a specialized (primarily histopathology) laboratory in Malawi cost US\$150,000 to set up; about half of this cost is in addition to the cost of training two technicians in other countries (Gopal, personal communication). The cost of training two technicians in other countries was a further US\$74,000.

CONCLUSIONS

The differential diagnosis of the child in the vignette at the beginning of this chapter, ranging from tuberculosis to lymph node cancer, was wide, and each diagnosis would have required completely different treatments and management. Most of the possible diagnoses were life threatening; without the appropriate treatment, the prognosis was poor. Conversely, with the right diagnosis and resultant treatment, the prognosis would have been good. The widespread availability of and timely access to good quality pathology, as described in the essential pathology package, would have provided that accurate diagnosis.

Key Messages

Pathology is a cross-cutting discipline upon which the other health disciplines depend and a crucial component in the care pathway. Pathologists are diagnosticians who, as part of the clinical team, play a key role in linking clinical services with laboratory services, providing leadership, and capitalizing on the opportunities arising from rapidly emerging new technologies. Pathology contributes to research in both communicable and non-communicable diseases, and it plays a central role in national policy planning.

Recommendations

Implementation of the essential pathology package is needed to address the lack of timely, accurate pathology in many LMICs; the rapidly increasing burden of noncommunicable diseases makes such implementation a priority. Our economic analysis shows that provision of the essential pathology package is affordable at approximately 6 percent of a hospital's budget. An integrated network is crucial to achieving the benefits of shared knowledge, expertise, communication, and economies of scale.

The sustainability and quality of the essential pathology package depends on investment in education and training and in appropriate emerging technologies, including LIS. Standards of practice need to be assessed across the network by an ongoing system of internal and

external (accreditation) audits. Reimbursement systems, especially for universal health coverage, need to include pathology to minimize out-of-pocket expenses and disincentives to appropriate use. Finally, ongoing research is important to obtain more accurate data on the economic benefits of pathology and on the most cost-effective solutions.

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046–US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126–US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

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