

From Morphology to Integrated Diagnosis: The Evolving Role of Pathology in Precision Medicine

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The history of medical diagnosis in modern medicine has always begun with observation. Hippocrates, 60 – 370 BC, observed the four humours of blood, phlegm, yellow bile, and black bile to help him in diagnosis. Prior to the emergence of laboratory technologies, clinicians relied on what they could appreciate by their naked eyes—the appearance of urine and stool, or the gross characteristics of an abnormal organ or lesion. With the development of microscopy in the 17th century, observation acquired a new dimension. Furthermore, with Rudolf Virchow’s “Cellular Pathology” concept, morphology became one of the foundational pillars of Pathology and continues to remain central to diagnostic practice.¹

However, disease diagnosis has never been confined to the morphology seen under the microscope. The advancement in the medical field is mainly due to incorporated information that could be measured rather than merely observed. Biochemical investigations provided insight into metabolic and functional disturbances through the analysis of blood and other body fluids. Hematological examination, immunological testing, and microbiological investigations added further dimensions to the understanding of disease. Histopathology brought together tissue architecture and cellular morphology, while advances in cytology provided valuable diagnostic information from individual cells and cellular populations. Each development expanded the diagnostic window rather than simply replacing what had existed before. The findings, when incorporated with the patient’s clinical presentations, helped significantly not only to understand the disease process, but also to the emergence of evidence-based treatment protocols.²

The emergence of immunohistochemistry marked another important transition in diagnostic Pathology. Immunohistochemistry not only gave the Pathologist confidence in the morphological diagnosis. Now, immunohistochemical markers are not only important in establishing diagnoses, as per WHO classification, but also in providing prognostic and predictive information. The question was never “What does the lesion look like?”, but “What does the lesion express, and what might that expression mean for the patient?”. Thus, Pathology is beyond the descriptive diagnosis and is a biological characterization.³

With the exponential growth of molecular pathology, this process has advanced even further. Techniques such as polymerase chain reaction, fluorescence-based assays and, more recently, next-generation sequencing have enabled the detection and characterization of molecular alterations underlying disease. With the identification of mutational signatures, we cannot only be aware of these carcinogens but also make our society aware of them. These developments have been particularly influential in oncology, where molecular findings may not only contribute to the classification, prognostication and therapeutic selection, but also to preventive action. The increasing availability of a wide range of genomic information has placed pathology at the centre of precision medicine,

where treatment decisions increasingly depend upon the biological characteristics of an individual patient's disease.⁴

Yet, the increasing sophistication of diagnostic technology presents an important paradox. This wide range of information does not necessarily equate to a better diagnosis and further management. Sometimes, this overinformation in the hands of a novice/inexperienced may lead to a catastrophe. A molecular alteration, immunohistochemical result, or biochemical abnormality cannot always be interpreted meaningfully in isolation. The significance of these findings should be correlated with the available clinical setting. The challenge of modern pathology is not to generate more data, but to determine which information is relevant and how different findings should be interpreted together to help in reaching the diagnosis and further management of the patient.⁵

This is where the concept of “Integrated Diagnosis” becomes important. Modern pathology is increasingly a process of bringing together epidemiological, clinical, morphological, hematological, biochemical, immunological, and molecular information to arrive at a coherent diagnosis. A pathologist is uniquely positioned at the intersection of these domains. Rather than being replaced by increasingly sophisticated technologies or even artificial intelligence, the role of the pathologist is consequently evolving from that of an observer of morphological abnormalities to an interpreter and integrator of diverse biological information.⁵

Pathologist of the future will therefore need to be comfortable both with the fundamentals of morphology and with rapidly advancing ancillary and molecular technologies. The ability to recognize a pattern under the microscope remains indispensable. However, the ability to understand when additional testing is necessary, how its results should be interpreted, and how those results alter the clinical understanding of disease has become undeniably necessary. Close communication with clinicians and participation in multidisciplinary decision-making will become increasingly important.⁵

The evolution of pathology should thus not be viewed as a journey in which morphology is progressively replaced by molecular diagnosis. Rather, it is an expansion of the diagnostic landscape—from observation to measurement, from characterization to molecular interrogation, and ultimately from individual test results to integrated interpretation. With advancements in science, newer technologies will continue to evolve and will help with precision. Amid this rapid progress, the central role of the pathologist will remain unchanged. The fundamental role of the pathologist is to transform complex biological information into a meaningful diagnosis that can guide patient care.

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