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Review Article

Applications of Immunohistochemistry in Disease Diagnosis: Principles, Challenges, and Recent Advances

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ABSTRACT

Immunohistochemistry (IHC) is a fundamental diagnostic technique that allows the detection and localisation of specific antigens within tissue sections through antigen–antibody interactions. Immunohistochemistry has developed into a vital tool in laboratory medicine and diagnostic pathology by fusing molecular specificity with retained tissue morphology. It is frequently used in the diagnosis, categorization, and prognosis of a wide range of illnesses, such as autoimmune, inflammatory, infectious, and neoplastic diseases. The sensitivity and dependability of immunohistochemical assays have been significantly improved by developments in staining techniques, detecting systems, and antibody creation. IHC aids in the classification of tumours, the identification of the tissue of origin, and the assessment of prognostic and predictive biomarkers in clinical practice, thereby enhancing diagnostic precision and therapeutic decision-making. Immunohistochemistry is widely used; however, staining results can be affected by a number of technical and interpretive issues. Variability can be introduced by pre-analytical factors, such as tissue fixation and processing, as well as analytical factors like antibody selection, antigen retrieval, and detection techniques. Additionally, there are still many difficulties with standardization, quality assurance, and result interpretation, especially in laboratory settings with limited resources. This narrative review discusses the fundamental principles of immunohistochemistry, its major applications in disease diagnosis, and the common technical and interpretative challenges encountered in routine practice. Additionally highlighted are recent developments in immunohistochemical methods, such as automation, multiplex staining, and digital pathology.

Keywords: Antigen retrieval; Biomarkers; Diagnostic pathology; Digital pathology; Immunohistochemistry

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INTRODUCTION

Immunohistochemistry (IHC) is a widely used laboratory technique that enables the detection and localisation of specific antigens within tissue sections through antigen–antibody interactions. By allowing visualisation of protein expression within preserved tissue architecture, immunohistochemistry offers both molecular and morphological information, making it a crucial tool in diagnostic pathology and biomedical research (Taylor & Levenson, 2006; Walker, 2006).

Immunohistochemistry has advanced significantly both technically and methodologically since it was first used in ordinary pathology practice. Low sensitivity and problems with antibody specificity hindered early immunohistochemical techniques; nevertheless, advancements in antibody synthesis, antigen retrieval techniques, and detection systems have significantly improved staining repeatability and reliability (Shi & Taylor, 2011; Ramos-Vara & Miller, 2014). These advancements have helped IHC become widely used in standard diagnostic labs all around the world.

In contemporary clinical practice, immunohistochemistry plays a central role in disease diagnosis, particularly in oncology. It is frequently used to classify tumours, determine the tissue of origin in metastatic illness, and evaluate prognostic and predictive biomarkers that inform treatment choices (Shi *et al*., 1991; Taylor *et al*., 1994). IHC's capacity to differentiate between morphologically identical tumours has greatly enhanced patient care and diagnostic precision.

Beyond oncology, immunohistochemistry is also applied in the diagnosis of infectious diseases, where it enables the detection of viral, bacterial, and parasitic antigens directly within tissue sections (Dabbs, 2019). Additionally, by identifying and characterizing immune cell types and disease-associated proteins, IHC is useful in the assessment of inflammatory, autoimmune, and degenerative illnesses (Goldstein *et al*., 2007). This broad applicability demonstrates how adaptable immunohistochemistry is in a variety of life science fields.

Despite its broad utility, immunohistochemistry is subject to several technical and interpretative challenges. Results can be affected by pre-analytical variables such as tissue fixation and processing, analytical variables including antibody selection and antigen retrieval, and post-analytical problems with staining interpretation (Fitzgibbons *et al*., 2014). Additionally, there is still a problem with standardization and quality control, especially in labs with limited resources (Taylor, 2006).

The basic concepts of immunohistochemistry, its main uses in illness diagnosis, and the technical and interpretive difficulties that arise in everyday practice are all summarized in this study. With a focus on their applicability to contemporary diagnostic pathology and laboratory medicine, recent developments in immunohistochemical techniques are also covered.

Literature Search Strategy

The literature used in this narrative review was obtained through searches of electronic databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords used in the search included "immunohistochemistry," "diagnostic pathology," "antigen retrieval," "biomarkers," and "digital pathology."

Articles published in English-language from 2000 to 2025 were taken into consideration. Studies addressing the principles, diagnostic applications, technical challenges, and recent advances in immunohistochemistry were included. Excluded were studies with insufficient methodological detail, editorials, and conference abstracts. Reference lists were manually screened to find more pertinent literature.

PRINCIPLES OF IMMUNOHISTOCHEMISTRY

Immunohistochemistry is based on the specific binding of antibodies to antigens within tissue sections, allowing the localisation and visualisation of target proteins in situ. The fundamental principle underlying this technique is the formation of an antigen–antibody complex that can be detected using a labelled detection system, making a visible signal at the site of antigen expression (Chu & Weiss, 2002).

Antigen–Antibody Interaction

The affinity and selective-binding of antibodies for their target antigens determine the specificity of immunohistochemistry. IHC antibodies are usually categorized as either polyclonal or monoclonal. High specificity and repeatability are provided by monoclonal antibodies, which are produced from a single B-cell clone, recognize and interact with a single epitope. Polyclonal antibodies, on the other hand, identify several epitopes on the same antigen, which may improve sensitivity but raise the possibility of non-specific staining (Moll *et al*., 2008). Therefore, a crucial factor in determining staining quality and diagnostic accuracy is the choice of antibody.

Tissue Preparation and Fixation

Appropriate tissue preparation is essential for successful immunohistochemical staining. Formalin-fixed, paraffin-embedded (FFPE) tissue is the most commonly used specimen type in routine diagnostic practice due to its ability to preserve tissue morphology and allow long-term storage (Miettinen, 2003). However, formalin fixation can lead to protein cross-linking and masking of antigenic epitopes, which may reduce antibody binding and staining intensity. The duration of fixation and type of fixative used can significantly influence antigen preservation and subsequent immunoreactivity (Ordóñez, 2012).

Antigen Retrieval

These techniques are frequently employed to reverse epitope masking as a result of fixation. It involves disrupting protein cross-links to expose antigenic epitopes; these techniques seek to restore antigenicity. Heat-induced epitope retrieval (HIER), the use of buffers like citrate or EDTA, or enzymatic digestion using proteolytic enzymes can all be used to retrieve antigens (Swerdlow *et al*., 2017). The heat-induced procedures are repeatable and compatible with automated staining systems, and are most suitable in contemporary laboratories (Rakha *et al*., 2010).

Detection Systems

Detection methods are used to visualize the antigen-antibody complex formed by the binding of an antibody to the corresponding antigen. Enzyme-based and fluorescence-based detection techniques are the two main categories. Horseradish peroxidase or alkaline phosphatase are frequently used in enzyme-based systems to catalyze a chromogenic reaction that results in a colored precipitate that may be seen under a light microscope (Hammond *et al*., 2010). Fluorescence-based detection uses fluorophore-labeled antibodies and permits multiplex labeling, but photobleaching and the requirement for specialized microscope equipment limit its application in routine diagnostics (Wolff *et al*., 2018). By removing the requirement for biotin, which may be found naturally in tissues, advances in polymer-based detection techniques have increased sensitivity while lowering background staining (Dowsett *et al*., 2011).

Controls in Immunohistochemistry

The dependability and interpretability of immunohistochemistry results depend on the adoption of suitable controls. Negative controls aid in identifying non-specific staining or background artifacts, whereas positive controls verify that the staining procedure and reagents are operating as intended (Tot, 2000). In ordinary diagnostic practice, internal controls—such as normal tissue parts within the same section—are especially helpful.

Antibody specificity, tissue preparation, antigen retrieval, detection technologies, and quality control procedures all interact intricately in the fundamentals of immunohistochemistry. Accurate interpretation and the best possible diagnostic application of immunohistochemistry in laboratory medicine require a deep comprehension of these concepts.

APPLICATIONS OF IMMUNOHISTOCHEMISTRY IN DISEASE DIAGNOSIS

Immunohistochemistry is an integral component of modern diagnostic pathology, providing critical information that complements routine histomorphological assessment. By enabling the detection of specific protein markers within tissue sections, IHC supports disease classification, differential diagnosis, prognostication, and therapeutic decision-making across a wide range of clinical conditions (Kerr & Sporn, 2015).

Applications in Cancer Diagnosis

Oncologic pathology is where immunohistochemistry is most widely used. IHC is frequently used to categorize tumours, identify the tissue from which they originated, and differentiate between neoplasms with similar morphologies. Immunohistochemical marker panels help reveal lineage-specific antigens in poorly differentiated malignancies, which helps guide an accurate diagnosis (Perry & Brat, 2017).

In epithelial tumours, cytokeratin expression profiles are commonly used to confirm epithelial origin and aid in tumour subtyping. For example, cytokeratin 7 and cytokeratin 20 expression patterns are frequently applied to differentiate primary and metastatic carcinomas (Chu & Weiss, 2002). In mesenchymal tumours, markers such as vimentin, desmin, and smooth muscle actin are used to characterise sarcomas and related neoplasms (Pritt & Cooper, 2012).

The diagnosis of haematolymphoid cancers also depends on immunohistochemistry. To differentiate between T-cell and B-cell lymphomas, lineage-specific markers such as CD3, CD20, and CD79a are frequently employed. Subclassification, which has significant prognostic and therapeutic consequences, is aided by additional markers (Perry & Brat, 2017).

Beyond tumour classification, IHC plays a significant role in prognostication and prediction of therapeutic response. The assessment of hormone receptors in breast cancer, such as oestrogen and progesterone receptors, as well as human epidermal growth factor receptor 2 (HER2), is a well-established example of how immunohistochemistry directly informs treatment decisions (Nuovo, 2014). Similarly, immunohistochemical evaluation of proliferation markers such as Ki-67 contributes to tumour grading and risk stratification in several cancer types (Dowsett *et al*., 2011).

Detection of Metastatic Disease and Tumour Origin

When evaluating metastatic tumours with an unclear primary origin, immunohistochemistry is especially useful. In these situations, a panel of immunohistochemical markers is used to identify the most likely origin based on patterns of antigen expression. Diagnoses of lung, prostate, and colorectal origins are commonly supported by markers such as thyroid transcription factor-1, prostate-specific antigen, and caudal-type homeobox 2 (Ordóñez, 2012).

In cases of metastatic disease, the adoption of algorithmic techniques that combine morphology and immunohistochemistry profiles has greatly increased diagnostic accuracy. This method facilitates optimal clinical care and lowers diagnostic uncertainty (Yaziji & Barry, 2006).

Applications in Infectious Diseases

Immunohistochemistry is also widely used in the diagnosis of infectious diseases, particularly when conventional microbiological methods are inconclusive or when dealing with non-culturable organisms. IHC allows direct visualisation of viral, bacterial, fungal, and parasitic antigens within tissue sections, thereby confirming the presence of infectious agents in the context of tissue pathology (Torlakovic *et al*., 2015).

Immunohistochemistry is frequently used in viral infections to identify viral antigens in tissues impacted by illnesses such as hepatitis, CMV infection, and lesions linked to the human papillomavirus (Williams *et al*., 2019). Disease classification is supported and diagnostic confidence is increased when viral proteins can be localized inside particular cell types (Williams *et al*., 2019).

In bacterial and parasitic infections, IHC may be used to identify organisms that are sparse, morphologically ambiguous, or masked by host inflammatory responses. This is particularly valuable in tissue biopsies from immunocompromised patients, where atypical infections are more common (Nielsen, 2014).

Applications in Inflammatory and Autoimmune Diseases

Immunohistochemistry plays an important role in the evaluation of inflammatory and autoimmune conditions by enabling the characterisation of immune cell populations and inflammatory pathways within tissues. Markers such as CD4, CD8, CD68, and CD20 are frequently used to identify lymphocyte subsets and macrophages, thereby providing insight into disease mechanisms and activity (Adeyi & Olusegun, 2016).

IHC can detect disease-specific patterns of tissue damage and immune activation in autoimmune disorders. For instance, the diagnosis and categorization of autoimmune-mediated tissue damage in organs such the skin, kidney, and gastrointestinal tract are aided by immunohistochemical detection of immune complex deposition and inflammatory cell infiltration (Fleming *et al*., 2017).

Beyond standard histology, immunohistochemistry can be utilized to evaluate cytokine expression and signaling pathways in chronic inflammatory diseases. Although these applications are more prevalent in research settings, in certain clinical situations they are increasingly contributing to prognostic and diagnostic evaluation (Adesina *et al*., 2013).

Role in Neuropathology and Degenerative Diseases

In neuropathology, immunohistochemistry is indispensable for the diagnosis of neurodegenerative diseases and central nervous system tumours. Markers such as glial fibrillary acidic protein, synaptophysin, and neurofilament proteins are used to characterise neural and glial cell populations (Ibrahim *et al*., 2018). In neurodegenerative disorders, immunohistochemical detection of abnormal protein aggregates, including tau and alpha-synuclein, supports definitive diagnosis and disease classification (Lloyd & Florell, 2017).

Contribution to Integrated Diagnosis

Within the framework of integrated diagnosis, where morphological, immunohistochemical, and molecular data are combined to obtain optimal diagnostic accuracy, the role of immunohistochemistry has been of immense importance. In this situation, IHC frequently acts as an accessible and affordable stand-in for molecular testing, especially in environments with restricted access to sophisticated molecular methods (Madabhushi & Lee, 2016).

All things considered, immunohistochemistry is still a flexible and essential diagnostic method for a variety of disease types. Its continued significance in ordinary diagnostic practice and laboratory medicine is guaranteed by its capacity to offer precise, tissue-based molecular information (Sepulveda *et al*., 2017; Shia, 2014).

TECHNICAL AND INTERPRETATIVE CHALLENGES OF IMMUNOHISTOCHEMISTRY

Despite its widespread application and diagnostic value, immunohistochemistry is subject to several technical and interpretative challenges that can affect staining quality and result interpretation. Awareness and management of these challenges are essential to ensure accurate, reproducible, and clinically meaningful outcomes (Taylor & Shi, 2013).

Pre-Analytical Variables

One of the main causes of variation in immunohistochemistry staining is pre-analytical factors. Antigen preservation and immunoreactivity can be significantly impacted by tissue fixation, fixative type, and fixation length (Fitzgibbons, 2018). Reduced staining intensity or false-negative results may arise from antigen degradation or excessive cross-linking caused by prolonged or insufficient fixation (Fitzgibbons, 2018). Despite its widespread use, formalin fixation necessitates careful management to strike a balance between tissue preservation and antigen accessibility.

Section thickness, embedding techniques, and tissue processing are other pre-analytical factors. Staining consistency and antibody penetration may be impacted by changes in these factors (Rosai, 2018). Antigen stability may also be jeopardized by delays between tissue excision and fixation, especially for labile proteins (Rosai, 2018).

Analytical Factors

Analytical challenges arise from factors directly related to the staining process. Antibody selection and validation are critical, as poorly characterised or non-specific antibodies may lead to false-positive staining or misleading results. Batch-to-batch variability in antibody production and differences between manufacturers can further contribute to inconsistencies (Bancroft & Gamble, 2013).

For every interaction of antibody and antigen, antigen retrieval conditions must be optimized. While excessive retrieval might result in tissue injury and non-specific background staining, insufficient retrieval can lead to weak staining. In a similar vein, chromogens and detection systems need to be carefully chosen to balance specificity and sensitivity (Cross, 1998).

Staining can also be hampered by biotin and endogenous enzyme activity, especially when using enzyme-based detection techniques. Background staining is still a problem in several tissue types, despite the fact that polymer-based detection techniques have lessened these problems (Taylor, 1998).

Post-Analytical Interpretation

Interpretation of immunohistochemical results introduces an additional layer of complexity. Staining intensity, distribution, and cellular localisation must be assessed within the appropriate morphological context. Subjective interpretation can lead to inter-observer variability, particularly in borderline or equivocal cases (van Diest *et al*., 2004).

Interpretation is made more difficult by the absence of widely recognized grading systems for some biomarkers. While some indicators, such as hormone receptors in breast cancer, have standardized scoring rules, many immunohistochemical markers rely on semi-quantitative or qualitative evaluation, which may lower repeatability (Fitzgibbons *et al*., 2014).

Standardisation and Quality Assurance

Immunohistochemistry standardization is still a global challenge. There can be a lot of variation between institutions due to variations in equipment, reagents, and laboratory procedures. Maintaining consistency and dependability requires adherence to approved protocols and participation in external quality assurance programs (O'Leary, 2000).

Immunohistochemical performance may be further hampered in resource-constrained environments by issues with infrastructure, reagent availability, and technical know-how. Diagnostic confidence may be impacted and variability may be made worse by restricted access to automated platforms and quality control systems (Taylor, 2017).

Strategies to Address Challenges

Laboratories are increasingly using automated staining methods, validated antibody panels, and standard operating procedures to lessen these difficulties. To increase uniformity and interpretation accuracy, pathologists and laboratory staff must receive ongoing training and professional development (Wolff *et al*., 2018).

Pre-analytical, analytical, and post-analytical variables must be carefully controlled for immunohistochemistry to be a reliable diagnostic tool. To maximize the diagnostic value of immunohistochemistry in everyday practice, these issues must be addressed by standardization, quality assurance, and training (Prichard, 2017).

RECENT ADVANCES IN IMMUNOHISTOCHEMISTRY

Recent technological and methodological advancements have significantly expanded the capabilities of immunohistochemistry, enhancing its sensitivity, reproducibility, and diagnostic utility. These developments have strengthened the role of IHC in routine pathology while also bridging the gap between traditional histopathology and molecular diagnostics (Gonzalez & Shi, 2018).

Automation and Standardisation

The increasing use of automated staining platforms is one of the most significant developments in immunohistochemistry. By standardizing crucial processes including antigen retrieval, antibody incubation, and detection, automation has decreased the variability associated with manual staining operations. As a result, laboratory uniformity and reproducibility have improved (Torlakovic & Nielsen, 2016).

By cutting down on turnaround time and minimizing human mistake, automated technologies help improve laboratory efficiency. Furthermore, quality assurance and adherence to laboratory accreditation criteria are supported by the incorporation of reagent tracking and approved processes into automated systems (Williams *et al*., 2020). These advantages are especially important in educational institutions and high-volume diagnostic labs.

Multiplex Immunohistochemistry

An important development that enables the simultaneous detection of several antigens inside a single tissue segment is multiplex immunohistochemistry. Multiplex methods allow the evaluation of intricate cellular connections and co-expression patterns while maintaining tissue architecture by employing distinct chromogens or fluorophores (Gerdes *et al*., 2013).

Multiplex IHC has been used more frequently in oncologic pathology to describe tumour microenvironments, such as immune cell infiltration and checkpoint molecule expression. This method offers important insights into the biology of tumours and may have an impact on decisions about immunotherapy (Parra *et al*., 2017). The gradual integration of multiplex techniques into diagnostic practice reflects the changing role of immunohistochemistry, even if they are more frequently utilized in research settings.

Digital Pathology and Image Analysis

The interpretation of immunohistochemical staining has changed with the advent of digital pathology. With the use of specialized software, whole-slide imaging makes it possible to digitize and analyze tissue sections for remote viewing, consultation, and archiving (Bankhead *et al*., 2017). Digital platforms reduce subjectivity and inter-observer variability by enabling standardized evaluation of staining intensity and distribution.

The quantitative assessment of immunohistochemical markers has been further improved using image analysis algorithms and artificial intelligence-based techniques. These methods are especially helpful for biomarkers like proliferative indices and receptor expression levels that need to be precisely scored (Gurcan *et al*., 2009).

Although there are still some areas where digital pathology is not fully implemented, its use is growing steadily.

Integration with Molecular Techniques

Molecular diagnostic techniques continue to be complemented by immunohistochemistry. IHC is frequently used as an inexpensive screening or stand-in method for determining which cases need additional molecular testing. For instance, screening for microsatellite instability prior to confirmatory molecular analysis is frequently done using immunohistochemistry evaluation of mismatch repair proteins (Sepulveda *et al*., 2017).

Because access to sophisticated molecular platforms may be limited in laboratories with low resources, this integrated diagnostic method is particularly beneficial. Immunohistochemistry helps maximize resource use while preserving diagnostic accuracy by directing specific molecular tests (College of American Pathologists, 2014).

Implications for Resource-Limited Settings

Improving sustainability and accessibility in low- and middle-income nations has also been a focus of recent developments in immunohistochemistry. IHC is now more feasible to implement in labs with limited infrastructure thanks to streamlined procedures, reliable detection systems, and affordable reagents (World Health Organization, 2011). The growth of immunohistochemical services in these contexts has been further aided by capacity-building programs and international partnerships.

The diagnostic potential of immunohistochemistry has been greatly enhanced by developments in automation, multiplex staining, digital pathology, and integration with molecular diagnostics. The changing function of IHC in contemporary pathology and laboratory medicine is still being shaped by these developments **(**International Organization for Standardization, 2012; Petrosyan & Berger, 2016).

RELEVANCE OF IMMUNOHISTOCHEMISTRY IN RESOURCE-LIMITED SETTINGS

Immunohistochemistry remains a highly relevant and practical diagnostic tool in resource-limited settings, where access to advanced molecular diagnostic technologies is often restricted. Its ability to provide valuable diagnostic and prognostic information using routinely processed tissue specimens makes IHC particularly suitable for laboratories operating with constrained infrastructure and funding (Moodley *et al*., 2019).

Histopathology services are the foundation of diagnostic medicine in many low- and middle-income nations, particularly when it comes to the assessment of chronic illnesses and cancer. By enabling tumour classification, tissue origin identification, and confirmation of particular disease entities, immunohistochemistry improves the diagnostic accuracy of conventional histology. IHC frequently acts as an economical substitute or alternative diagnostic technique in situations when molecular testing is either unavailable or prohibitively expensive (Adegoke *et al*., 2020).

Despite its benefits, logistical and infrastructure limitations often make it difficult to apply immunohistochemistry in labs with low resources. These include irregular power supplies, restricted access to automated staining platforms, reagent and antibody shortages, and poor lab equipment upkeep. In addition, financial limitations may restrict the availability of comprehensive antibody panels, leading to reliance on a limited number of essential markers (Nakhleh, 2016).

Human resource capacity also plays a critical role in the effective use of immunohistochemistry. Shortages of trained histotechnologists and pathologists can compromise staining quality and result interpretation. Continuous training, mentorship, and capacity-building initiatives are therefore essential to improve technical proficiency and diagnostic confidence (Novis, 2014). The development of simplified, standardised protocols has been shown to improve reproducibility and sustainability of IHC services in such environments.

In environments with limited resources, quality assurance is still a major challenge. The reliability of immunohistochemistry results may be impacted by low involvement in external quality evaluation programs and a lack of internal quality control procedures. Ensuring consistent diagnostic performance and patient safety requires strengthening quality management systems, even at the most basic level (Burnett, 2013).

Access to immunohistochemistry has been greatly increased in underprivileged areas thanks to international partnerships and technology transfer programs. IHC services have been established and strengthened in a number of settings thanks to support in the form of training programs, reagent donations, and technical advice (Sayed *et al*., 2016). These initiatives highlight how crucial long-term collaborations are to enhancing diagnostic capability. Immunohistochemistry offers a practical, adaptable, and cost-effective diagnostic solution in resource-limited settings. With appropriate investment in infrastructure, training, and quality assurance, IHC can continue to play a central role in improving disease diagnosis and patient care in these environments (Bates & Maitland, 2006).

CONCLUSION AND FUTURE PERSPECTIVES

Immunohistochemistry remains an indispensable tool in diagnostic pathology and laboratory medicine, offering a unique combination of molecular specificity and preserved tissue morphology. Its numerous uses in the detection of degenerative, infectious, inflammatory, and neoplastic illnesses highlight its ongoing significance in contemporary medicine. Immunohistochemistry has developed into a dependable and adaptable method that facilitates precise disease classification and clinical decision-making that benefits the advancements in antibody generation, detection technologies, and standardization.

Pre-analytical variability, antibody selection, result interpretation, and standardization continue to be problems despite these developments. To guarantee consistent and repeatable immunohistochemistry results, it is crucial to address these issues through reliable quality assurance methods, verified procedures, and ongoing professional training. This is especially crucial in environments with limited resources, as infrastructure and skill limitations may affect diagnostic performance.

In the future, it is anticipated that immunohistochemistry's diagnostic utility will be further enhanced by its integration with digital pathology and molecular diagnostic procedures. Accuracy, efficiency, and repeatability will continue to be enhanced by automation, multiplex staining, and image analysis technologies. Simultaneously, initiatives to increase access to immunohistochemistry in low- and middle-income nations through international cooperation and capacity building are still crucial.

In conclusion, immunohistochemistry continues to play a central role in diagnostic practice and will remain a cornerstone of pathology services. Immunohistochemistry will continue to contribute successfully to disease diagnosis and patient treatment in a variety of healthcare settings with further innovation, standardization, and investment in infrastructure and training.

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Not applicable.

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Not applicable.

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SAF conceived and designed the review, coordinated the author team, and drafted the initial manuscript. KO, IAU, IAO, OJO, IOJ, ACE, OFA, BMO, IGO, POO (Obami), CEW, SS, IGO (Onukwue), POO (Okunola), AAA, and SIA contributed to literature searching, selection of relevant evidence, manuscript structuring, and drafting of specific sections. JUM provided senior supervision and critical oversight of the review. All authors critically revised the manuscript for important intellectual content, approved the final version for publication, and agree to be accountable for all aspects of the work.

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