Contents

Preface: Artificial Intelligence in the Clinical Laboratory **ix**

Jason M. Baron

Artificial Intelligence in the Clinical Laboratory: An Overview with Frequently Asked Questions **1**

Jason M. Baron

This article provides an overview of machine learning fundamentals and some applications of machine learning to clinical laboratory diagnostics and patient management. A key goal of this article is to provide a basic foundation in clinical machine learning for readers with clinical laboratory experience that will set them up for more in-depth study of the topic and/or to become a better collaborator with computational colleagues in the development and deployment of machine learning–based solutions.

Electronic Health Record Optimization for Artificial Intelligence **17**

Anand S. Dighe

Laboratory clinical decision support (CDS) typically relies on data from the electronic health record (EHR). The implementation of a sustainable, effective laboratory CDS program requires a commitment to standardization and harmonization of key EHR data elements that are the foundation of laboratory CDS. The direct use of artificial intelligence algorithms in CDS programs will be limited unless key elements of the EHR are structured. The identification, curation, maintenance, and preprocessing steps necessary to implement robust laboratory-based algorithms must account for the heterogeneity of data present in a typical EHR.

Clinical Artificial Intelligence: Design Principles and Fallacies **29**

Matthew B.A. McDermott, Bret Nestor, and Peter Szolovits

Clinical artificial intelligence (AI)/machine learning (ML) is anticipated to offer new abilities in clinical decision support, diagnostic reasoning, precision medicine, clinical operational support, and clinical research, but careful concern is needed to ensure these technologies work effectively in the clinic. Here, we detail the clinical ML/AI design process, identifying several key questions and detailing several common forms of issues that arise with ML tools, as motivated by real-world examples, such that clinicians and researchers can better anticipate and correct for such issues in their own use of ML/AI techniques

Artificial Intelligence Applications in Clinical Chemistry **47**

Dustin R. Bunch, Thomas J.S. Durant, and Joseph W. Rudolf

Artificial intelligence (AI) applications are an area of active investigation in clinical chemistry. Numerous publications have demonstrated the promise of AI across all phases of testing including preanalytic, analytic, and

postanalytic phases; this includes novel methods for detecting common specimen collection errors, predicting laboratory results and diagnoses, and enhancing autoverification workflows. Although AI applications pose several ethical and operational challenges, these technologies are expected to transform the practice of the clinical chemistry laboratory in the near future.

Digital Health: Today's Solutions and Tomorrow's Impact **71**

Alison Hellmann, Ashley Emmons, Matthew Stewart Prime, Ketan Paranjape, and Denise L. Heaney

Artificial intelligence (AI) is becoming an indispensable tool to augment decision making in different health care settings and by various members of the patient pathway, including the patient. AI provides the ability to optimize data to bring clinical decision support for clinicians and laboratorians and/or empower patients to actively participate in their own health care. Though there are many examples of AI in health care, the exact role of AI and digital health solutions is still taking shape. Although AI will not replace the clinician, those who do not adopt AI may in time, be left behind.

Opportunities and Challenges with Artificial Intelligence in Genomics **87**

Danielle E. Kurant

The development of artificial intelligence and machine learning algorithms may allow for advances in patient care. There are existing and potential applications in cancer diagnosis and monitoring, identification of at-risk groups of individuals, classification of genetic variants, and even prediction of patient ancestry. This article provides an overview of some current and future applications of artificial intelligence in genomic medicine, in addition to discussing challenges and considerations when bringing these tools into clinical practice.

Using Artificial Intelligence to Better Predict and Develop Biomarkers **99**

Sam A. Michelhaugh and James L. Januzzi Jr.

Advancements in technology have improved biomarker discovery in the field of heart failure (HF). What was once a slow and laborious process has gained efficiency through use of high-throughput omics platforms to phenotype HF at the level of genes, transcripts, proteins, and metabolites. Furthermore, improvements in artificial intelligence (AI) have made the interpretation of large omics data sets easier and improved analysis. Use of omics and AI in biomarker discovery can aid clinicians by identifying markers of risk for developing HF, monitoring care, determining prognosis, and developing druggable targets. Combined, AI has the power to improve HF patient care.

Laboratory Aspects of Minimal / Measurable Residual Disease Testing in B-Lymphoblastic Leukemia **115**

John Kim Choi and Paul E. Mead

Minimal residual disease detection provides critical prognostic predictor of treatment outcome and is the standard of care for B lymphoblastic

leukemia. Flow cytometry–based minimal residual disease detection is the most common test modality and has high sensitivity (0.01%) and a rapid turnaround time (24 hours). This article details the leukemia associated immunophenotype analysis approach for flow cytometry–based minimal residual disease detection used at St. Jude Children's Research Hospital and importance of using guide gates and back-gating.

Artificial Intelligence in the Genetic Diagnosis of Rare Disease **127**

Kiely N. James, Sujal Phadke, Terence C. Wong and Shimul Chowdhury

The use of Natural Language Processing (NLP) and Artificial Intelligence (AI) have been introduced into various areas of medicine with the hopes of eliminating human bias, increasing accuracy, and efficiently deploying the medical workforce. With the incorporation of whole exome sequencing (WES) and whole genome sequencing (WGS) into the clinical setting in recent years, NLP and AI tools have been developed to help support the extensive manual effort required to analyze large amounts of genomic data. This chapter will summarize current tools and approaches of NLP and AI, and provide examples of how these tools can aid in the scalability and application of genomic medicine into clinical practice.