The small numbers of medicine and the big numbers of artificial intelligence: a curated-data approach to appropriateness in laboratory medicine and coagulation

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ABSTRACT

Inappropriateness in medical decision-making remains a persistent challenge, particularly in laboratory medicine. This phenomenon is largely driven by cognitive inadequacy, defined as the growing mismatch between the exponential expansion of medical knowledge and the limited capacity of human cognition to assimilate and apply it in real time. Artificial intelligence (AI), especially in its narrow form, designed and trained to perform specialized tasks, offers practical tools to mitigate this gap. This article examines the potential role of AI in improving prescription appropriateness in laboratory medicine, with a focus on coagulation diagnostics, and proposes a novel AI-based system that supports physicians at the point of decision-making through the use of curated, expert-annotated data.

Key words: artificial intelligence, appropriateness, blood coagulation.

Introduction

Already in the first century AD, Seneca and Lucretius reflected on *res novae et inusitatae* when compared to scientific and intellectual innovation. In the 21st century, artificial intelligence (AI) represents a similarly disruptive response to cognitive inadequacy, which is recognized as a major determinant of prescriptive inappropriateness in medicine. This article focuses on inappropriateness in laboratory medicine, with particular attention to blood coagulation testing, a field characterized by complex diagnostic pathways and rapidly evolving knowledge. Over the past decade, AI has demonstrated expert-level performance across multiple medical domains. In 2017, AI systems achieved expert-level performance in radiographic pneumonia diagnosis,[1] in 2018, in melanoma detection and retinal imaging,[2,3] in 2020, in mammography analysis and in the discovery of the first antibiotic developed using deep learning.[4,5] By 2025, AI systems were capable of complex clinical reasoning.[6]

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A recent landmark achievement

A landmark achievement was the awarding of the 2024 Nobel Prize in Chemistry to Hassabis, Jumper, and Baker for advances in three-dimensional protein structure prediction using AlphaFold2 model which allows to predict the 3D protein's structure within minutes.[7] These achievements were enabled by three pivotal factors: large-scale biological data (big data), advances in machine learning algorithms, and high-performance computing, which allow the processing of massive datasets through complex algorithms. It is foreseeable that, despite its lights and shadows,[8,9] AI will profoundly transform laboratory medicine as well as the management and understanding of thrombosis and hemostasis,[10,11] as briefly outlined in this article.

In a previous investigation,[12] AI was defined in an innovative way as "a discipline that studies and develops systems capable of performing tasks requiring a form of intelligence and improving cognitive adequacy" emphasizing its role in enhancing cognitive adequacy.

Artificial narrow intelligence (ANI) addresses this limitation by managing mechanical knowledge at a scale and complexity unattainable by earlier decision support systems and expert systems.[13,14] ANI refers to AI systems which are limited in scope, being designed to perform a specific task or a set of closely related tasks. It operates under a predefined set of rules and its capabilities are limited by predefined functions, lacking the capacity to apply knowledge to different contexts beyond its specific domain, thinking abstractly or having emotional intelligence. ANI, combined with machine learning techniques such as deep learning, can adapt to processed data, enabling the analysis of large datasets, pattern recognition, and data-driven predictions or decisions.[15]

Mechanical knowledge can be illustrated by an analogy: when perceiving the scent of an iris, the mechanical process of cognition involves the interaction of odorant molecules with nasal chemoreceptors, signal transmission to the olfactory bulb and neocortex, and the association of that scent with the image of an iris. The emotional response elicited by the scent, and the subjective awareness of its meaning, belong instead to the domain of consciousness, which is beyond the scope of this work.

Medical knowledge is largely *mechanical*, particularly in laboratory medicine, radiology, pathology, molecular biology, and genetics where interaction with patients is limited or absent. A major source of cognitive inadequacy arises from inefficient postgraduate knowledge transmission and the overwhelming volume of scientific literature. Recently, COVID-19 pandemic, exemplified how continuous revision of medical knowledge is necessary.

Two main factors hinder adequate learning for medical decision-making: the enormous amount of scientific data published each year across thousands of journals, and the limitations of the human neural system, shaped by evolution over tens of thousands of years and poorly adapted to exponential data growth.[16-19] While it is difficult to objectively measure a physician's knowledge, AI systems can be benchmarked using thousands of test items.

Inappropriateness and cognitive inadequacy

Human cognitive inadequacy is indirectly demonstrated by the extensive literature on medical error management.[20,21] A proxy measure of cognitive inadequacy is prescriptive inappropriateness. Literature reports inappropriate prescription rates of approximately 15-50% in laboratory medicine, 50% in pharmacology, and 20-40% in radiology.[22-28] The level of inappropriateness in the use of D-dimer for excluding deep vein thrombosis is one of the most obvious examples.[29]

Despite originating from different disciplines, and although each discipline may have distinct contributing factors, these values converge on a common underlying cause: cognitive inadequacy. These data indicate that traditional professional development methods are inefficient, particularly when rapid clinical decisions are required. Such decisions are further compromised by cognitive biases, memory limitations, and human error.

AI can provide knowledge precisely when it is needed by: i) generating new knowledge; ii) reorganizing existing but fragmented physician knowledge while mitigating bias; iii) providing feedback that confirms existing knowledge.[30]

A novel pyramid of knowledge

Before the advent of AI, the prescribing process could be represented as a pyramid,[31] in which complexity is positioned at the top and synthesis and decision-making at the bottom (Figure 1).

A practical example may help to clarify this concept and its graphical representation. When a physician suspects antiphospholipid syndrome and wishes to prescribe tests to confirm the diagnosis, his cognitive system formulates the following ques-

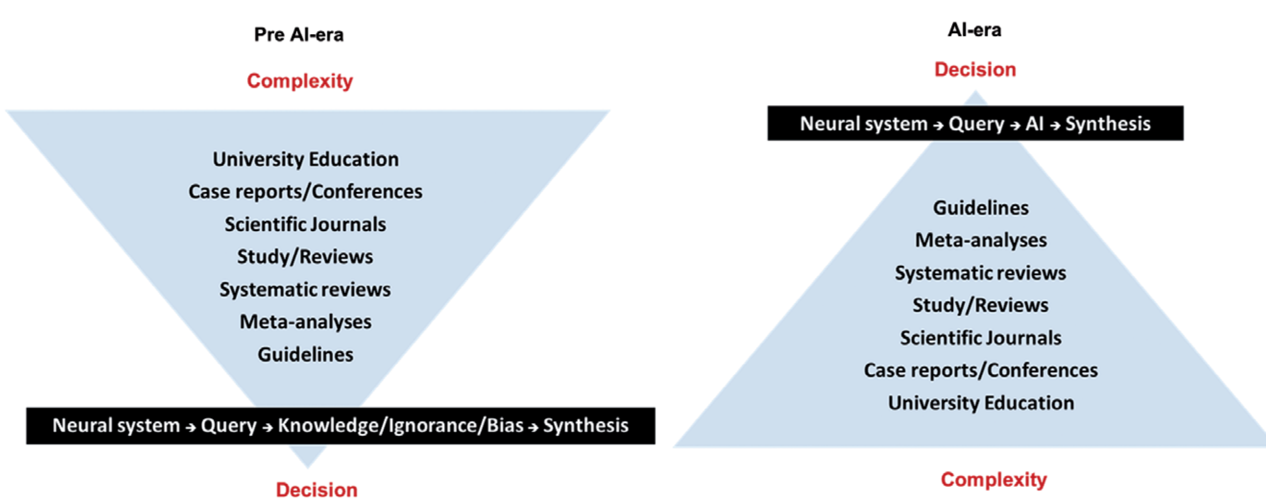

Figure 1. By representing the decision-making process as a pyramid, in pre-artificial intelligence (AI) era, complexity is positioned at the top, while synthesis and decision-making at the bottom. In the AI era, the pyramid is inverted, with complexity positioned at the bottom, while synthesis and decision-making at the top. Compared to the pre-AI era, AI helps reduce cognitive biases, memory limitations, and human error.

tion: which tests should be prescribed to diagnose antiphospholipid syndrome?

The answer is generated by passing through multiple layers of knowledge, represented at the base of the pyramid in their full complexity. These include undergraduate medical education, which should constitute the foundational infrastructure of knowledge, and postgraduate training, progressively enriched by clinical cases, conferences, scientific journals, original studies, reviews, systematic reviews, meta-analyses, and clinical guidelines.

This process produces the knowledge of that specific physician at that specific moment, which is necessarily partial and incomplete. Moreover, as with all humans, it is affected by cognitive biases and limitations, including automatisms, lapses, memory gaps, prejudices, and general reasoning fallacies.[32] With the introduction of AI, the pyramid is inverted, with complexity positioned at the bottom and synthesis and decision-making at the top.

The physician still formulates the clinical question, but the response no longer passes through the previously described layers of complexity. Instead, it is directly provided by artificial intelligence as mechanically generated knowledge, for example: lupus anticoagulant, anti-cardiolipin antibodies IgG and IgM, and anti–beta2 glycoprotein I antibodies IgG and IgM.[33]

At this stage, the physician remains free to accept or reject the proposed recommendation.

In this process, cognitive biases and reasoning fallacies related to information overload, structural limitations of the human cognitive system, or insufficient knowledge may be bypassed, and relevant information can be delivered precisely at the moment of need.

AI can achieve this synthesis because medicine operates on relatively small datasets, whereas AI systems are designed to handle large-scale data. For example, laboratory tests number in the thousands,[34] active pharmaceutical ingredients about 2900,[35] recognized diseases number approximately 2000,[36] and rare diseases around 10,000.[37] These quantities exceed the capacity of the human neural system. In contrast, AI systems operate at the scale of billions of parameters and data points.

From a technical regulatory perspective, AI systems used in medicine must comply with the EU AI Act (2024) and ISO/IEC 42001:2023 for AI applications, which requires algorithmic transparency, data quality, human supervision, and digital CE marking.[38,39]

Artificial logic for medicine appropriateness

We propose a novel AI system based on deep neural networks inspired by biological neuroscience, here referred to as Artificial Logic for Medicine Appropriateness (ALMA). Deep learning employs multilayered artificial neural networks trained to perform tasks such as classification and pattern recognition. The main components of these networks are nodes and weights. Nodes act as computational units that receive data, combine it mathematically, and transmit processed signals to subsequent layers. Weights are adjustable numerical parameters that regulate the strength of connections between nodes and determine how strongly each laboratory parameter influences the final diagnostic output. The proposed model is suggested to be based on *discriminative* AI, which is characterized by supervised learning using labelled data where both input data and labels are available during training. The focus is on minimizing classification errors or maximizing the probability of accurate class predictions using back-propagation, gradient descent optimization, and regularization to adjust the decision boundary and obtain optimal classification accuracy.

ALMA would then integrate both discriminative and narrow AI, which often complement each other or overlap, as the latter delineates scope and competence of the system, while the former defines methods and functionality.[40]

As tangible examples, among several coagulopathies, we consider thrombophilia and von Willebrand disease (VWD) (Figures 2 and 3). The input layer consists of all available clinical pathology tests. Expert clinicians, using consolidated scientific knowledge, label tests relevant or irrelevant to each diagnosis or clinical condition. We in fact believe that supervised learning, employing hand-annotated or curated data by experts,[41,42] provides the best quality guarantees for a high-risk AI system to be used in healthcare.[38]

Unlike existing medical-content applications available on the internet, which are largely based on the mere collection and organization of data, this approach is not a low-cost solution. Rather, it represents a deliberately high-investment model that provides prescribers with greater safety and a reduction in errors. Crucially, it enables an active role for scientific societies in recruiting expert specialists for the annotation of clinical practices and for their continuous revision in line with the evolution of scientific knowledge.[31] Some tests may have multiple labels reflecting their involvement in different pathological contexts. For example, antithrombin carries at least two labels, as it is involved in both thrombophilia and hepatic conditions, whereas platelets, which are implicated in a wide range of clinical situations, may carry dozens. With a prompt such as *useful tests for thrombophilia diagnosis,* the system outputs the relevant diagnostic tests (output layer). A similar model applies to hemorrhagic disorders such as VWD.

To comply with the EU AI Act, test labelling must be performed by recognized academic and medical experts, periodically updated, and globally applicable. Although the initial complexity is high, the long-term benefit lies in structurally reducing prescriptive inappropriateness while preserving physicians' critical thinking.

Conclusions

We therefore believe that AI can serve as an effective tool to address cognitive inadequacy, contributing to a more appropriate and improved practice of medicine. At present, however, AI remains a tool that requires careful management and which cannot replace human judgment and creativity, but it can augment clinical reasoning by managing complexity beyond human cognitive limits. As AI continues to advance, it raises important questions about the future of work, privacy, ethics. The pyramidal complexity in the pre-AI era, illustrated at the base of Figure 1, should not be viewed negatively, as human reasoning does not operate according to binary logic, and this intrinsic complexity forms the foundation of critical thinking that enables the effective and responsible use of AI in medicine.

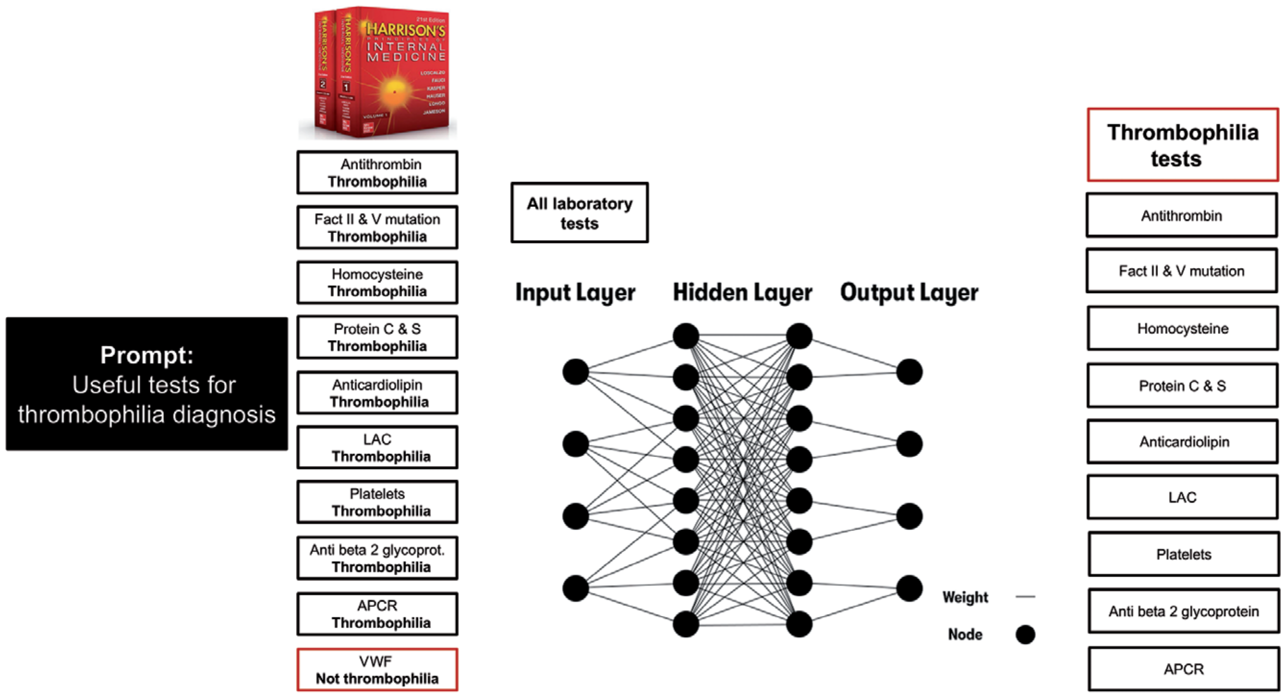

Figure 2. Architecture of a deep neural network trained on curated laboratory data for thrombophilia diagnosis. Individual laboratory tests are represented as input nodes, which are connected through weighted links to hidden layers. These weights are optimized during training to capture relevant diagnostic patterns. Given the specific prompt (useful tests for thrombophilia diagnosis) the output layer provides probability estimates for thrombophilia-related diagnostic tests.
LAC, lupus anticoagulant; APCR, activated protein C resistance; VWF: von Willebrand Factor.

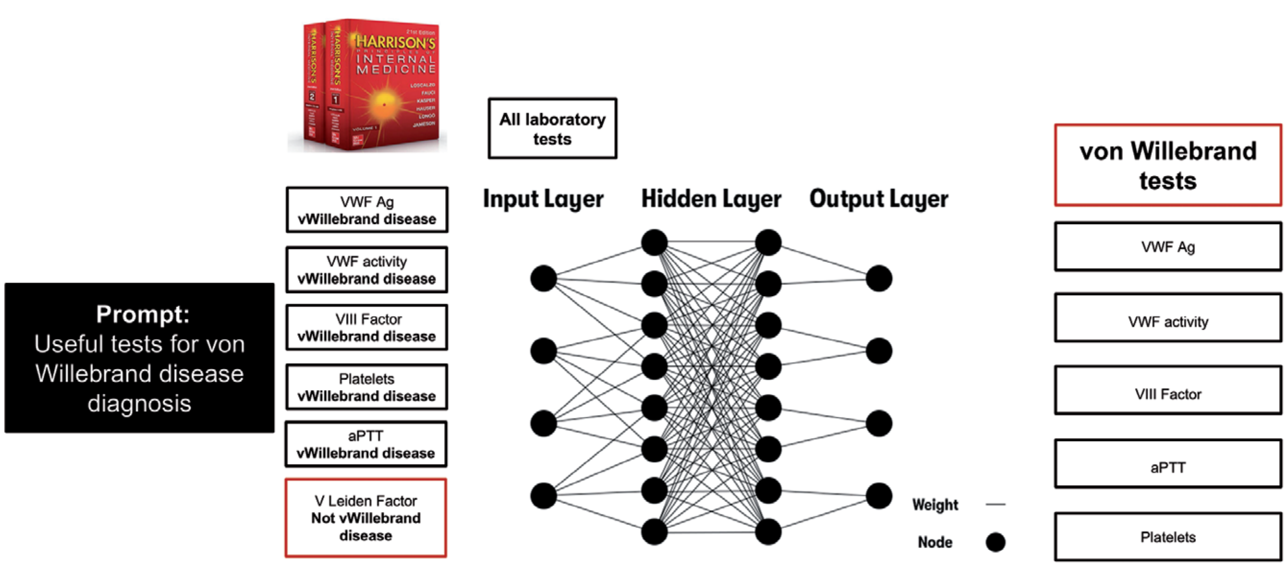

Figure 3. Architecture of a deep neural network trained on curated laboratory data for von Willebrand disease diagnosis. Individual laboratory tests are represented as input nodes, which are connected through weighted links to hidden layers. These weights are optimized during training to model complex relationships among laboratory parameters. Given the specific prompt (useful tests for von Willebrand disease diagnosis) the output layer provides probability estimates for von Willebrand disease-related diagnostic tests.
VWF, von Willebrand Factor; aPTT, activated partial thromboplastin time.

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