

Medical Education

The challenge of medical diagnosis: A primer on principles, probability, process and pitfalls

K.S. JACOB

ABSTRACT

Arriving at a medical diagnosis is a complex process, which requires clinical skill. However, the need for clear decisions has to be balanced by an acceptance of the ambiguity of many clinical situations. Complex presentations often require probabilistic inferences rather than presumed diagnostic certainty. The demands, logic and process of clinical diagnosis are highlighted. The multiple aspects of clinical reality and the impact of gold standards, nature of evidence and dichotomous disease/no disease categorization are discussed. The importance of population characteristics and context in diagnosis and prediction are emphasized. The statistics of agreement, Bayesian approach, certainty and risk, hazards and pitfalls, common errors, audit and the influence of commercialization on diagnosis are addressed. There is a need to formally teach the art and science of medicine and to transfer clinical skill rather than hope that such skills will be automatically imbibed during training.

Natl Med J India 2015;28:24–8

INTRODUCTION

Most patient–physician interactions result in a medical diagnosis or are a follow-up on decisions made. Diagnostic conclusions are routine in clinical practice, have major implications for patients and determine subsequent therapy. However, many physicians rarely appreciate the complexity of the process, which is also frequently misunderstood by patients. Most medical teachers fail to explicitly transfer skills related to clinical diagnosis to their students. The belief that these skills are imbibed and need not be formally taught reflects a lack of understanding of principles and practice of the science and the art of clinical medicine. It suggests poor comprehension of medical logic, probability and diagnostic certainty. This article discusses various issues related to clinical diagnosis and their implications.

THE CLINICAL DEMANDS

A physician is required to make clear decisions based on an unambiguous estimate of the patient's problem. Patients seek and physicians usually provide such a definitive diagnosis, which works well in practice. However, often, the clinical picture is ambiguous, making it difficult to reach a definitive conclusion. In such situations, the possibility of making a mistake is real and is a common professional hazard for all physicians. Rather than accepting the ambiguity of some clinical situations and explaining

this to patients, physicians may make definitive decisions in unclear circumstances. Situations, which demand a probabilistic inference due to the incomplete and fragmentary nature of the available information, are discussed in terms of clinical certainty, forcing errors.

The logic of clinical diagnosis

Formal logic is deductive. For example, two plus two is always four within the closed systems of mathematics. In contrast, inductive logic (Bayesian), used in clinical diagnosis, does not have the same degree of certainty. It moves from a set of facts or observations to a general conclusion. For example, all observed crows are black; so all crows must be black. Such a conclusion is convincing and probable, but not necessarily factual or binding. Conclusions drawn from studying problems in a series of 100 patients with a particular disease are used to diagnose and predict issues in the hundred and first patient presenting with similar problems. Such a process is inherently prone to error.

The diagnostic process

The traditional view of the diagnostic process is that it is one of analytical reasoning. It includes the generation of hypotheses, their testing and verification based on patient data, through a conscious deductive process (called the hypothetico-deductive method).^{1,2} The physician identifies the clinical problem and generates one or more diagnostic hypotheses. She then searches for clinical information to confirm a particular hypothesis generated and refute others. Consequently, the diagnostic process appears to shift from the use of inductive logic to a process of deduction. For example, if a patient has a clinical condition X, then he must have its characteristic features. Generating a number of hypotheses early in the diagnostic process and using them to guide data collection to find solutions to complex clinical problems is useful.

Nevertheless, a detailed analysis of the diagnostic method fails to explain many aspects of the process.^{2,3} How are some clinicians able to suggest tentative hypotheses about the diagnosis? How do these 'experts' generate conjectures based on minimal information and without conscious awareness of the retrieval process? Recent research argues for non-analytical reasoning among skilled physicians, based on pattern recognition, a process that is intuitive and that matches the clinical pattern with memory.^{2,3} The speed, accuracy and efficiency of the diagnostic process among 'experts' argues against the routine use of the hypothetico-deductive method for common clinical situations. Pattern recognition is used for solving common clinical presentations, while clinical reasoning is usually reserved for complex and ambiguous presentations.

The ability to categorize a set of objects allows us to apply knowledge learnt to a potentially infinite class of new, previously

Department of Psychiatry, Christian Medical College, Vellore 632002, Tamil Nadu, India; ksjacob@cmcvellore.ac.in

unseen material. Categorization allows clinicians to extrapolate information previously learnt and apply it to new patients and contexts. Cognitive research suggests two mechanisms involved in such categorization.^{2,3} The prototype theory argues that the person's experience with examples of the condition are averaged into a composite prototype of the category, which contains most classical and critical features of the group. It then allows for a feature-by-feature match of the new patient with the prototype. The second mechanism, called the exemplar theory, suggests an unconscious match to previously known examples of such categories. The second process is holistic and does not use a sequential analysis of the characteristic features; experience with classic examples allows for categorization through an unconscious process, which matches their similarity.

Clinicians seem to use both processes in arriving at a diagnosis. Novices tend to use feature-by-feature prototype match. However, the acquisition of clinical expertise through practical experience allows for a greater use of holistic matching of similarity with exemplars. 'Expert' clinicians seem to identify additional features to complete the clinical picture and relate findings to the overall concept of the case. Experts seem to construct a diversified and abstract network of links between clinical features and a particular diagnosis.²

Research into clinical processing also suggests the role of encapsulation and packaging of the detailed information and their interrelationships into a smaller number of higher-level concepts with the same explanatory power.⁴ For example, a clinical presentation of fever, chills, breathlessness, sweating and prostration associated with a rapid pulse and low blood pressure are encapsulated in the concept of sepsis. This abstraction not only identifies the clinical constellation but also its pathophysiology. Such clinical constructs (contextualized narrative structures referred to as illness scripts)⁴ allow for holistic evaluations of syndromes and identify simplified causal mechanisms.

The diversity of clinical problems mandates a flexible approach; clinical expertise and experience dictates choice of strategies.

Clinical reality and gold standards

The standards for diagnosis of varied diseases are different. While some conditions are diagnosed on the basis of pathology obtained by biopsy, others rely on clinical signs or radiological and laboratory tests, which are surrogate markers for tissue pathology. For example, marked cerebral atrophy on brain scans in people with severe memory loss and multiple cognitive impairments supports the possibility of a diagnosis of dementia even in the absence of information from a brain biopsy. While the documentation of cerebral pathology through brain biopsy would be ideal to confirm a diagnosis of dementia, it is not practical and current gold standards for the diagnosis rely on a combination of clinical symptoms, neuropsychological tests and laboratory investigations, as a proxy for diagnosis.⁵

Definite, contributory and surrogate evidence

The evidence generated by medical procedures contributes different weights to diagnosis. Certain procedures, such as a liver biopsy for hepatitis, produce definitive evidence. Other procedures, such as the elevation of the enzyme creatinine phosphokinase in patients with suspected myocardial infarction, provide contributory evidence. When combined with a clinical history and electrocardiographic data, the results of the test can lead to a diagnostic decision. There are many easy and inexpensive procedures, which are surrogate and substitute for more definitive tests, and are used to screen for

different conditions. Those positive on such screens are subsequently confirmed using expensive or elaborate tests.

Dichotomous thinking and dimensional reality

The results of many clinical assessments and diagnostic tests used in medical practice are sharply divided as positive or negative. Despite its mathematical and clinical convenience, dichotomous demarcations often misrepresent clinical reality, which can lie on a spectrum, leading to errors.⁶ Clinical phenomena located midway on the spectrum pose problems when classified into two categories. Although dimensions have been postulated for many clinical phenomena, they are difficult to handle in practice and hence categorical approaches are preferred.^{7,8} However, the advantages of continuums and the convenience of clinical categories can be achieved if trichotomous categorizations involving three zones of operations are employed (e.g. positive, negative and equivocal).⁶

The categorization of the continuum of delusion (e.g. normal thought through overvalued ideas to morbid beliefs) into three zones will help the accuracy of the definitive zones while the equivocal response will demand additional testing.^{7,8} Uncertainty in the elicitation of delusions commonly attributed to inexperience is not imperative and doubtful phenomena are part of clinical practice and should be labelled as such. Similarly, the separation of epileptic seizure from pseudo-seizures is based on clinical details. Clinical presentations with definitive epileptic seizures and classical hysterical seizures at either ends of the clinical spectrum also mean a mid-zone of diagnostic uncertainty.

The dimensional spectrum of plasma glucose concentration is another example. Past approaches to diagnosis of diabetes mellitus used a threshold of 126 mg/dl for dichotomous demarcation into a diabetic and normal range for blood sugar. Modern standards use a trichotomous division. A fasting blood sugar level between 100 and 125 mg/dl (5.6 and 6.9 mmol/L) is considered pre-diabetes. If it is 126 mg/dl (7 mmol/L) or higher, a diagnosis of diabetes is in order.⁹

Using trichotomous categorization of dimensional reality increases the diagnostic accuracy of the positive and negative zones. Additional information such as the presence or absence of other psychotic phenomena (e.g. hallucinations or grossly abnormal behaviour) can be used to alter the probability of delusional thinking when patient evaluation suggests the ambiguous nature of beliefs. Similarly, the results of an electroencephalogram (EEG) can alter the probability of epileptic/pseudo-seizures to confirm the type of seizures in people assessed to be on the mid zone of the clinical spectrum. Likewise, results of glycosylated haemoglobin provide additional context for impaired plasma glucose concentrations.

Statistics of agreement and of prediction

A surrogate or screening diagnostic test is judged by its agreement with the gold standard. Many tests have reasonable indices or averages, which reflect the number of people with disease who are identified by the clinical or laboratory test (sensitivity) and the number of people without disease who are test negative (specificity).⁶ However, the predictive value of a test, when applied in practice, is dependent on the prevalence of the condition in the population tested.⁶

Tests used in groups of individuals with a low prevalence of the condition to be detected would produce high false-positive rates. For example, diagnostic tests such as venereal disease research laboratory (VDRL) test for syphilis, when employed indiscriminately, will result in poor prediction and errors. The test

should only be applied in patients who report a history of unprotected sexual exposure, as this would artificially raise the prevalence of the condition in the group being tested. Similarly, indiscriminate use of screening tests in groups with a very high possibility of a condition (e.g. using the VDRL test in patients with clear signs of neurosyphilis) results in high false-negative rates.

The importance of context

The ability to focus on important clinical issues and see the big picture requires clinicians to separate the wheat from the chaff. Experts realize that the context has a more powerful influence on diagnosis than clinical data. Often, the probability of a common disease presenting in an atypical fashion is higher than that of a rare disorder. Knowledge of the background of a patient (e.g. age, sex, family history) and local conditions (e.g. geographic location, travel, socioeconomic status, site of lesion) make it possible to reach the correct diagnosis. For example, the high prevalence of tuberculosis in India and many low- and middle-income countries would argue for the need to exclude the condition for clinical presentations with poor appetite and loss of weight even in the absence of the more classical symptoms of fever and cough.

Population characteristics

The principles of elicitation of signs during the clinical examination are comparable to those used to interpret diagnostic laboratory tests in medicine. The indices of efficacy of a diagnostic test (i.e. sensitivity and specificity) are generally considered constant.⁶ However, this assumption is valid only when the test and population characteristics remain stable. Thus, clinical characteristics that are useful indications in particular populations may prove inaccurate in others. For example, a negative purified protein derivative (PPD) test does not imply the absence of tuberculosis in children with Kwashiorkor and severe protein-energy malnutrition. Poor immune responses in such conditions do not allow for a positive test even in the presence of tuberculosis. Similarly, the denial of persecutory delusions in a paranoid individual would not necessarily imply the absence of such pathology. The generalization of paranoid ideation in such patients, who incorporate the interviewer into their belief system and are non-cooperative for the clinical examination, would result in their denial of persecutory beliefs.^{7,8}

Children with Kwashiorkor and patients with severe paranoid illness differ markedly from normal populations and hence behave differently on tests useful in routine clinical practice. Variations commonly seen in patients demand an understanding of issues.

Bayesian approach

Clinical examination essentially uses a Bayesian approach for the identification of clinical phenomena and diagnosis. It depends on acknowledging the examiners belief about the patient's clinical state (prior probability) before data on a specific aspect is available and modifying it to reach a conclusion (posterior probability). Thus, sociodemographic and contextual characteristics, history and general impressions during clinical examination are used to assess the pre-test probability related to the presence of a particular diagnosis. The specific symptoms and clinical signs elicited and results of laboratory tests are used to modify this prior probability to reach a conclusion about pathology.

The clinician's assessment of disease probability in the individual tested is important. There should be a reasonable uncertainty about the presence or absence of the disease before the surrogate test is ordered for the most optimal interpretation of test

results. For example, patients with recurrent classical generalized tonic-clonic (grand mal) seizures may have normal surface EEG recordings suggesting a false-negative result. Epilepsy is a clinical diagnosis and sole reliance on EEG findings is bound to result in errors.

The clinician's estimate of disease probability is crucial. The probability of the disease before the use of a test would have to be assessed and the test used in situations where the pre-test probability lies in the range of 0.4–0.6. There should be a reasonable uncertainty about the presence or absence of the disease before the test is ordered for the most optimal interpretation of test results. Diagnostic tests should be selected and administered in such a way as to influence the clinician's estimate of pre-test probability of disease.

Certainty and risk

The degree of diagnostic certainty needed in making clinical decisions is also a function of the degree of risk presented by therapeutic options. For the use of specific therapy, which is highly efficacious and has a low risk of adverse effects (e.g. the use of vitamin supplementation in pregnancy), few tests are needed because physicians can accept substantial diagnostic uncertainty. On the other hand, in situations where treatment options are less effective and have a greater risk of adverse effects (e.g. in cancer), clinicians often need a higher degree of diagnostic certainty. Physicians and patients should also realize that the judicious use of second opinions in situations, where the implication of diagnostic procedures, the diagnosis and treatment are grave, may be necessary.

Hazards and pitfalls

The complexity of the diagnostic process and medical inference demands caution and wisdom.² On one hand, thorough data collection does not preclude ignoring or misinterpreting clinical findings, while on the other, data collection in situations of limited availability of information can still allow for accurate interpretation and correct diagnosis. Initial diagnostic hypotheses generated for complex clinical presentations may not include the correct solution; unusual clustering of symptoms and syndromes may impede pattern recognition making restructuring of information challenging. Physicians should beware of their propensity to commit to a particular diagnosis early in the course of the diagnostic process in demanding cases, which makes reformulation difficult.

Deconstructing complex processes suggests the need to pursue and identify parsimonious, economical and succinct explanations with the fewest assumptions (Occam's razor). Nevertheless, more complicated solutions may ultimately prove correct, and will also need to be considered supporting the counter-argument commonly known as Hickam's dictum (often stated as 'patients can have as many diseases as they damn well please') and its place in clinical diagnosis.

Physicians often have deeply entrenched individual mind-sets that value the production of evidence-supported narratives of diseases. They may handle information and reach conclusions, without necessarily examining the probabilistic nature of the process of diagnosis. Nevertheless, clinical diagnosis involves the drawing of probabilistic inferences based on incomplete and fragmentary information in order to support decision-making.

Common errors

There is a need to recognize common errors in the cognitive

Guidelines for improving diagnostic skill

1. Accept that the need for clear clinical decisions has to be balanced by the recognition of the ambiguity of many clinical situations.
2. Acknowledge that complex presentations often require probabilistic inferences rather than presumed diagnostic certainty.
3. Recognize common clinical patterns seen in practice and match them with clinical presentations; use hypothetico-deductive method in complex cases.
4. Categorize and weigh the evidence into definite, contributory and surrogate classes.
5. The context and population characteristics impact statistics of agreement and prediction (sensitivity, specificity, predictive values and false rates) and demand caution in interpretation.
6. The Bayesian approach used for diagnosis is prone to error and mandates frequent reappraisal and audits.
7. 'Good' clinicians regularly review patient data, revalidate the patterns identified, examine probabilities and question their earlier diagnostic interpretations, thus reassigning risks and re-evaluating diagnoses.
8. Skills related to diagnosis in medicine should be formally taught in medical school.

process, which often lead to incorrect diagnosis. These include (i) availability heuristic (clinicians judge the likelihood of a particular diagnosis by how easily examples spring to mind); (ii) anchoring heuristic (physicians stick with initial impressions); (iii) framing effects (people make different decisions based on how information is presented); (iv) blind obedience (trainees stop thinking when confronted with authority); and (v) premature closure (when several possible options are not pursued).¹⁰ These common errors should be discussed during training.

Looking forward, looking back

Expert clinicians understand the limits of inductive logic, the often inconclusive nature of the evidence and ambiguous clinical presentations and their impact on diagnosis and consequent prognostication. They regularly review the evidence, consider possible differential diagnoses, employ probabilistic inference and plan for diverse outcomes for unclear presentations.

The question to be asked is: 'Will an audit find evidence of best practice?' An appraisal of the evidence and the diagnostic process in each case, as done in a formal review, is crucial. This is particularly necessary for diagnostic and management decisions with serious clinical implications, grave prognosis and those with possible medicolegal connotations. A treatment plan covering all possible differential diagnoses and their management is mandatory in complicated cases. Regular reevaluation for all patients should become a routine practice and clinical lifestyle.

Hindsight and diagnosis

A perfect diagnostic system does not exist; improvements often result from a trade-off. Highly sensitive systems over-diagnose conditions while blunter investigative methods under-estimate the risks. The trade-off is essentially between sensitive systems, which give false alarms, and blunt systems, which do not pick up the condition concerned. The diagnostic challenge for physicians is to separate the signal from background noise.

A missed diagnosis is always clear in hindsight. The thread connecting relevant information, which was missed or misinterpreted, can be found but before the final discovery, the big picture may form an indistinct pattern. This has been described as 'creeping determinism' where the occurrence of an event increases its reconstructed probability and makes it less surprising than it would have been had the original probability been kept in

mind. Such creeping determinism later becomes unfair criticism of the diagnostic process. In practice, clear diagnostic stories may be less frequent than realized. Nevertheless, medical negligence needs to be differentiated from errors made due to the ambiguity of the clinical situation.

The impact of commercialization

The commercialization of healthcare has had a major impact on diagnostic testing. Commissions for doctors for ordering tests have resulted in indiscriminate and inappropriate use of many investigations. These have resulted in increased cost of healthcare and greater psychological stress from false-positive diagnosis for patients while increasing incomes for physicians and hospitals. False-positive tests, common in situations of indiscriminate diagnostic testing in contexts of low prevalence, can distort diagnostic reasoning and complicate clinical decisions. The practice of defensive medicine in legally fraught contexts has a similar impact on the decision-making process.

IMPLICATIONS FOR MEDICAL EDUCATION

The exposure to exemplars for pattern recognition is crucial to learning. Consequently, the need for rote learning of classical signs and symptoms of particular disease (e.g. pulmonary tuberculosis) needs to be de-emphasized. Memorization of common differential diagnosis for specific presentations (e.g. headache) can also be futile. The availability of and exposure to many similar typical examples will facilitate appropriate pattern recognition.² Such expertise can only be gained as a result of extensive experience, the consequence of deliberate practice.

Non-analytical reasoning, crucial to success for medical diagnosis, needs to be emphasized and discussed during medical training, without belittling mechanism-based physiological analysis. There is a need to encourage students to use both non-analytical reasoning and analytical knowledge. The principles, practice, probability, process and pitfalls should be formally taught and be part of the medical curriculum. While the use of diagnostic checklists has increased reliability of medical diagnosis, they have not reduced the importance of understanding clinical reasoning and probability in the diagnostic process. Ticking boxes is no substitute for clinical skill. The need to move from mainly collecting data to considering diagnostic possibilities is part of the journey from novice to expert.

Medical schools need to facilitate the acquisition of clinical

experience. Basic sciences should be taught in a clinical context; patient problems, biomedical and psychosocial knowledge, exemplars and prototypes and the processing of clinical information should be introduced early in training and as part of an integrated teaching curriculum. Students should be guided through the different transitory stages in developing expertise. They need to be educated on the components required to achieve expertise in medical diagnosis: knowledge expansion and restructuring, pattern recognition, understanding causal networks and pathophysiological processes that explain causes and consequences.⁴ Clerkships during the medical course with small group discussions facilitated by an 'expert' clinician will aid in acquiring the necessary skills. Many of these issues have also been discussed in the popular press¹¹ and should be essential reading for physicians and for patients.

Good teachers not only use these principles in their clinical practice but also demonstrate them to their students. Discussing clinical presentations, highlighting different aspects of the diagnostic process, demonstrating pattern recognition and matching, encouraging students to shift from a feature-by-feature comparison to holistic matching and generating and confirming/refuting hypotheses for complex cases is necessary. Identifying common errors, hazards and limitations of the diagnostic technique as part of regular audit empowers students. Emphasizing the need for periodic assessments in every case is mandatory. Leading by example and verbalizing technique sets a good teacher apart from the average one.

CONCLUSION

Physicians often value the production of evidence-supported narratives of diseases. They rarely examine the probabilistic nature of the process of diagnosis. All physicians make mistakes, have weaknesses and expertise is not a static but dynamic state. Experienced clinicians regularly review patient data, revalidate the patterns identified, examine probabilities and have the courage to question their earlier diagnostic interpretations allowing them to reassess risks and diagnoses. Some clinicians fail to understand the process and repeatedly make the same errors in judgement.

There is a need to refocus on improving clinical skills and on the judicious use of diagnostic tests. The journey to becoming an experienced clinician is not for the impatient and is a continuous quest for improvement.

Problem-solving and decision-making in clinical medicine are complex processes. They often involve the simultaneous use of multiple strategies including pattern recognition and hypothesis testing. Diagnostic categorization involving pattern recognition uses both exemplars and abstract clinical prototypes. Complex clinical presentations mandate the generation of multiple diagnostic hypotheses, appropriate collection of evidence and testing. Experienced clinicians follow patterns of symptoms to make appropriate conclusions of disease. They do so by reversing the approaches adopted in medical texts, which are often organized around disease categories rather than on clinical presentations. The challenge is to integrate the science and the art of clinical medicine. Understanding the diagnostic process can help physicians make the best decisions related to health.

REFERENCES

- 1 Elstein AS, Shulman LS, Sprafka SA. *Medical problem solving: An analysis of clinical reasoning*. Cambridge, MA:Harvard University Press; 1978:64–6.
- 2 Elstein AS, Schwartz A. Clinical problem solving and diagnostic decision making: Selective review of the cognitive literature. *BMJ* 2002;**324**:729–32.
- 3 Norman G, Young M, Brooks L. Non-analytical models of clinical reasoning: The role of experience. *Med Educ* 2007;**41**:1140–5.
- 4 Schmidt HG, Rikers RM. How expertise develops in medicine: Knowledge encapsulation and illness script formation. *Med Educ* 2007;**41**:1133–9.
- 5 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders, Fifth edition*. Arlington VA:American Psychiatric Association; 2013.
- 6 Feinstein AR. *Clinical epidemiology: The architecture of clinical research*. Philadelphia:WB Saunders; 1985.
- 7 Jacob KS. Mental state examination: The elicitation of symptoms. *Psychopathology* 2003;**36**:1–5.
- 8 Jacob KS. Psychiatric assessment and the art and science of clinical medicine. *Indian J Psychiatry* 2012;**54**:184–7.
- 9 American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;**37** (Suppl 1):S81–S90. Available at http://care.diabetesjournals.org/content/37/Supplement_1/S81.full (accessed on 18 May 2014).
- 10 Redelmeier DA. Improving patient care. The cognitive psychology of missed diagnoses. *Ann Intern Med* 2005;**142**:115–20.
- 11 Groopman J. *How doctors think*. New Delhi:Byword Books; 2009.