Diagnostic error is common, with significant misdiagnosis occurring in 5%–15% of retrospectively analysed hospital presentations,1 and revealed in 9% of general hospital postmortem examinations.2 The rate of misdiagnosis in the complex, fast paced critical care environment may be higher still, with significant discrepancies between clinical diagnosis and postmortem findings occurring in up to 26% of intensive care autopsies.3 It could be argued that these postmortem-based results may be biased by the tendency to conduct autopsy in cases of the greatest clinical uncertainty. However, it is concerning that such a large proportion of patients die of illnesses for which the treatment and outcome may have been altered if the correct diagnosis had been made earlier. Consequently, there is growing interest in the root causes of misdiagnosis, and the means by which these may be addressed.

ABSTRACT

Misdiagnosis of the cause of illness in critically ill patients is common, and a major cause of morbidity and mortality. We reflect upon a misdiagnosis that occurred in the intensive care unit of a metropolitan teaching hospital, and highlight the susceptibility of medical decision making to error. We examine recent advances in cognitive theory and how these apply to diagnosis. We discuss the vulnerability of such processes and — with particular reference to our case — why even knowledgeable and diligent clinicians are prone to misdiagnose. Finally, we review potential solutions, both educational and systemic, that may guard against the inevitable failings of the human mind, especially in a busy modern intensive care setting.

Box 1. A misdiagnosed case

A 48-year-old woman with severe type 1 respiratory failure was admitted to the intensive care unit of a metropolitan teaching hospital. She presented to the emergency department with a few days’ history of general unwellness, fevers and increasing shortness of breath. In the days before the illness, she had been clearing pigeon nests from the loft of a building. Her earlier history included repair of aortic coarctation in infancy (reportedly resulting in a residual cardiac murmur) and hepatitis C infection. Examination revealed extensive bilateral crepitations and a pansystolic murmur. Initial laboratory investigations were unremarkable, with a normal C-reactive protein level and white cell count. A chest x-ray (Figure 1) showed widespread interstitial change in both lungs. The working diagnosis was atypical pneumonia, or pneumonitis secondary to a viral infection or pigeon-related allergic reaction. Empirical antimicrobials were commenced, the advice of respiratory and infectious disease specialists was sought, and supportive therapy was provided as required. Microbiological and virological testing yielded no positive results.

Despite aggressive intervention, the patient’s condition deteriorated. After a week, formal echocardiography was performed to assess cardiac function. An unexpected finding was severe mitral regurgitation, with an estimated systolic pulmonary artery pressure exceeding 100 mmHg. The diagnosis was revised to pulmonary oedema and pulmonary hypertension secondary to acute mitral regurgitation. The cause of mitral valve dysfunction was unclear. Nitric oxide therapy was initiated, and emergency mitral valve repair was performed when pulmonary artery pressure allowed. Valve replacement surgery was technically successful, and the patient returned to the ICU on only moderate haemodynamic support. Unfortunately, about 12 hours after the operation, there was a rapid deterioration in cardiovascular indices and worsening hyperkalaemia despite ongoing haemofiltration. Noradrenaline requirements reached 80 μg/min. Identification and correction of a surgical precipitant was deemed the only chance of survival, so resternotomy was performed in the ICU. However, no surgically correctable cause of deterioration was identified, refractory ventricular fibrillation ensued, and the patient died soon afterwards. The presumptive diagnosis was refractory systemic inflammatory response syndrome secondary to cardiopulmonary bypass in a patient with preoperative multiorgan dysfunction.

Figure 1. Chest x-ray showing widespread interstitial change in both lungs.
Using the case described in Box 1, we illustrate current cognitive theory relating to diagnosis and diagnostic errors.

The dual process model

Misdiagnosis may be attributed to a lack of factual knowledge, failure to gather information or failure of the cognitive process. Analysis of a series of 90 misdiagnoses in internal medicine revealed that 80% of the errors committed were the result of cognitive process failure. Understanding the mechanism of cognitive process failure, and the manner in which such failures may be avoided, first requires an explanation of the principles of human judgement and decision making.

Understanding of human judgment and decision making has traditionally involved two opposing schools of thought: one proposing that judgement is based primarily on rational thought and reason, the other championing a more automatic, intuitive process. Within the past 30 years, these views have been combined into a widely accepted theory known as the “dual process model”. This model, pioneered by Nobel laureate Daniel Kahneman, is based on a number of psychological experiments demonstrating the existence of two independent thought mechanisms: one rapid and intuitive (designated “system 1”), the other slow and rational (“system 2”) (Table 1).

System 1 is low-effort, near automatic, and responsible for the majority of everyday judgements. It relies on heuristics (pattern recognition and “rules of thumb”) to produce rapid answers that are of sufficient accuracy to manage the low-stakes decisions made throughout life. The recognition of a familiar face, the application of car brakes in response to a hazard on the road, the detection of hostility in a voice — all occur quickly, without our explicit awareness. System 1 rapidly compares environmental information with data stores acquired from education and experience and produces a response. It is a cognitive process that allows us, with minimal mental expenditure, to negotiate the millions of judgements and decisions that confront us throughout life. However, efficiency comes at a cost. The pattern recognition mechanism is subject to a multitude of subconscious biases; accuracy is often impaired. System 1 is therefore unsuitable for situations in which the stakes are high and precision is required.

System 2, by contrast, is the analytical and reasoned thought process used when novel situations are encountered (and thus no comparable pattern exists) or when the situation is deemed too complex or the stakes are too high for the automatic system. System 2 employs rules and logic and, as it does not rely on contextual environmental cues, may operate at a hypothetical level. However, such thinking places a significant burden on short-term working memory and requires expenditure of significant energy. As a result, system 2 is prone to disruption by competing cognitive demands and fatigue. Therefore, although more reliable and able to cope with complex or novel situations, system 2 is subject to fatigue and distraction.

The functional distinction between system 1 and system 2 is further supported by evidence from functional magnetic resonance imaging studies showing that the two systems use different parts of the brain, and by physiological data that demonstrate differences in energy requirements between the two means of thinking. The two systems do not, however, operate in isolation. System 2 is believed to cross-check and modify the output of system 1, adding reason and logic to intuitive (but potentially inappropriate) decisions. Equally, system 1 may influence system 2, its intuitive input providing a starting point for the logical processing of a complex problem.

Applying the dual process model to diagnostics

The advent of the dual process model led to advancement of the theory of diagnosis. Theories regarding diagnosis had, like their more general cognitive counterparts, been largely divided into two camps: the hypothetico-deductive method and the pattern-recognition method. The hypothetico-deductive model proposes that, when presented with a collection of symptoms, clinicians formulate a range of differential diagnoses; base further history, examination and investigation on these options; and, as further information becomes available, accept or refute options until a single, plausible diagnosis is reached. This approach was not universally accepted; investigators reported analysis of diagnostic practice that appeared out of keeping with a deductive process and more in line with direct automatic retrieval, or pattern recognition. It is now believed that both models of diagnosis are correct and that clinicians may use either or
both routes when confronted with a clinical presentation.

The parallel between these diagnostic theories and the dual process model is clear: pattern recognition equates with system 1 and the hypothetico-deductive model with system 2. The presumed role that each system plays in a given presentation, and the interaction between the systems, is illustrated in Croskerry’s model of diagnostic reasoning (Figure 2).13 If the pattern of presentation is easily recognisable to the clinician, system 1 will provide a rapid diagnosis with minimal cognitive effort. For example, a painful vesicular rash in a dermatomal distribution suggests, for most clinicians, a system 1 diagnosis of shingles. The likelihood of a presentation pattern being immediately recognisable depends on the number of diagnostic “templates” available to system 1. Thus, experts are more likely than novices to use system 1.10 In presentations in which no pattern is recognised, the more labour-intensive, hypothetico-deductive system 2 is initiated. Logic and rules are employed and potential diagnoses (which may in part be intuitively provided by system 1) are challenged or supported by collecting further information.

Output from both systems is cross-checked in a function described as “calibration”, and system 2 is capable of overriding system 1 in a “surveillance” or “governor-like” fashion.13,14 Additionally, repeated use of system 2 for a particular presentation is believed to lead to development of a template, allowing activation of system 1 in future cases.14

In summary, two cognitive pathways are available for diagnosis. The effort-light but bias-prone system 1 is the default if the pattern of presentation appears to fit available templates. System 2 plays the lead role in cases in which pattern recognition does not immediately provide a diagnosis.

Bayesian theory and diagnostic error

In its purest form, diagnosis is an act of applied probability. Any given presentation (eg, chest pain) will raise the possibility of numerous diagnoses (eg, myocardial ischaemia, pulmonary embolism or oesophageal rupture). The probability of these diagnoses is initially determined by incidence within the population — for example, myocardial ischaemia is common but oesophageal rupture is not. This is the pre-test probability. The emergence of further information allows revision of the probability, the extent of the revision being dependent on the strength of the new evidence (the likelihood ratio). For example, the additional information that the chest pain radiates into the arm, or is associated with ST segment changes on an electrocardiogram, increases the probability that the pain is due to ischaemia and reduces the probability that it is due to oesophageal rupture. This post-test probability then becomes the pre-test probability for the next stage; further appropriate information is sought (eg, the presence or absence of elevated plasma troponin levels); and the process is repeated until the probability of one pathology become sufficiently high to confidently make a diagnosis and initiate treatment.

The mathematical model relating to applied probability is Bayes’ theorem,10 and its sequential, logical, rule-based approach would seem a perfect fit for system 2. However, system 2 is labour-intensive, and prone to failure in times of fatigue or cognitive overload. Thus, whenever possible, diagnosis is the domain of system 1. Even when a conscious system 2 approach is used, significant input is received from system 1. The ability of system 1 to apply Bayes’ theorem is notoriously poor, and appreciation of the probability of events or diagnosis is particularly susceptible to its biases.5

There are even literary examples of system 1 succumbing to bias. In the novel The house of God,15 a medical student is berated for naming amyloidosis as the cause of renal dysfunction with the iconic line, “[T]ypical ... [when] a medical student hears hoofbeats outside his window, the first thing he thinks of is a zebra”. This human tendency to think of zebra when we hear hoofbeats, amyloid when we hear kidney failure or — as in the above case study — extrinsic allergic alveolitis when we hear shortness of breath is not explicable by logic or mathematical probability, but can be explained by our cognitive mechanisms and the biases to which they are susceptible.

Heuristics and bias

Availability heuristic

When considering the probability of an event (or diagnosis), the perceived likelihood will be influenced by the ease with
which the event comes to mind (the “availability heuristic”).\(^5\) The patient in the above case presented in winter, after several recently reported cases of influenza A pneumonia and in the midst of governmental campaigns raising awareness of the virus. The cold weather of winter is a positive predictor of influenza and should certainly have been integrated into the Bayesian logic in support of such a diagnosis. However, the repeated cognitive exposure of clinicians to the concept of influenza would also have resulted in availability heuristic, falsely increasing the perceived probability of the diagnosis.

**Confirmation bias**
When a hypothesis is formed, there is a tendency to seek evidence that confirms this and ignore evidence to the contrary. This is believed to be due to the human need to defend one’s feeling of competence and situational control.\(^16\) In this case, once the diagnosis of pneumonia or pneumonitis had been made, the natural tendency was to ignore factors disputing the diagnosis (eg, normal C-reactive protein level, negative microbiological tests).

**Anchoring**
“Anchoring” is the act of locking onto prominent features of the initial presentation, and failing to adjust one’s impression of events in light of later information.\(^17\) The clinicians in the above case are likely to have anchored on the exposure to bird nests and the (low-probability) associated diagnoses.

**Base rate neglect**
Bayesian logic suggests that the starting probability of any diagnosis is its prevalence within the population: this is the base rate. “Base rate neglect” is the act of hearing hoofbeats and thinking of zebra, of making an unusual diagnosis that ignores the most likely cause of the patient’s symptoms. Therefore, despite the fact that the patient in this case had been exposed to bird nests before becoming ill — which added weight to the case for diagnosing psittacosis or allergic alveolitis — cardiogenic pulmonary oedema is a far more common cause of hypoxia and bilateral crepitations, even in people exposed to pigeons. However, system 1 is prone to ignore such statistical information.

**Representativeness**
Although the templates on which system 1 operates will usually provide an accurate diagnostic match, there is a risk of failure if the presentation is not “classical”. There is thus a tendency to miss atypical presentations of disease. Had the patient in this case been elderly, with risk factors for cardiovascular disease, she may have better fitted the classic presentation for cardiogenic pulmonary oedema. However, the woman who presented in this case did not fit the picture, and system 1 consequently discounted this diagnosis.

**Premature closure**
The tendency to stop thinking when a diagnosis is made, even when not all information has been gathered and analysed, accounts for a significant proportion of misdiagnoses.\(^17\) This tendency is presumably a means of preserving finite cognitive resources.

**The avoidance of diagnostic error**
Recognition of the role of the biases discussed above, and many others, in the aetiology of diagnostic error has prompted a search for ways of protecting clinicians from weaknesses in cognitive processing. Eradication of system 1 thinking is not the aim:\(^18\) intuitive, automatic cognition rapidly provides an array of potential diagnoses and is, particularly in the hands of expert clinicians, often accurate. Rather, by acknowledging the potential failings of system 1, and implementing educational and systemic strategies to safeguard against these vulnerabilities, it may be possible to reduce the incidence of misdiagnosis.

Numerous authors have proposed educational strategies for reducing the impact of cognitive bias.\(^17,19-23\) These centre on metacognition: the understanding of one’s cognitive processes and strategies. Educating clinicians about the biases and heuristics to which they are susceptible potentially allows more reflective diagnostic practice to occur. It is suggested also that clinicians should apply a systematic approach to diagnosis (eg, an anatomical approach to chest pain or a prerenal, intrarenal and postrenal approach to renal failure\(^22\)) and, where feasible, Bayesian logic (ideally using statistical data gleaned from epidemiological studies rather than the clinician’s intuitive judgement).

Taking frequent “time-outs” to evaluate emerging information and challenging diagnoses that are not in keeping with all the data may guard against many heuristic practices, particularly if conducted in conjunction with other clinicians. Indeed, questioning a diagnosis and refining the differential list should be considered not only acceptable but desirable. Time-outs empower all parties to safely volunteer information and question decisions and encourage co-responsibility rather than leader-driven decision making. The ICU post-admission ward round may provide an ideal setting for conducting a team-wide review of available facts and considering how closely these match the classical presentation of the current diagnosis. Discussing and debating the clinical facts and potential diagnoses in an open manner that values contributions from multiple disciplines and personnel seems likely to protect against “blind spots” or potential biases that any one clinician may possess. Comparison to a “gold standard” also serves to
identify areas of residual uncertainty that may be targets for further investigation, or to stimulate a broadening of diagnoses.

Systemic changes also have a role to play. Checklists and diagnostic pathways encourage a systematic approach and incorporate Bayesian theory, one successful example being the Wells score for diagnosis of pulmonary embolism.24 The potential for checklists to reduce the risk of clinical error is increasingly recognised.25 However, unless they are well constructed and implemented with some degree of consensus and adequate education in their use, they are at risk of failure.26 Furthermore, with the ever growing number of checklists and pathways, there is a risk of “checklist fatigue”.27 This may explain the variable willingness of clinicians to use such decision-making tools.27

The ultimate application of logic to diagnosis would be implementation of computer-based diagnostic decision pathways, thus eliminating the human tendency towards bias.20 Introduction of such systems has led to improvements in clinicians’ performance,28 but no definitive improvement in patient outcomes.29 In their current stage of evolution, computer-based diagnostic tools are considered by many clinicians to be disruptive to workflow and cost-ineffective.20

Conclusion
By the very nature of human cognition, clinicians, regardless of the extent of their knowledge or the diligence with which they conduct their practice, are prone to errors of diagnosis. Accepting this vulnerability and appreciating the underlying mechanisms may provide some protection against error. But, until technology advances to the point that our cognitive processes are eliminated entirely from the act of diagnosis, there remains the risk that the mental short cuts bestowed on us by evolution will continue to attribute those hoofbeats heard through the window to zebra.

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References