We have recently proposed that diagnosis is a 3 step process which consists of suspecting, testing and inferring a disease in a patient (1). In this paper, we shall discuss the first step of suspecting a disease from a presentation, which we have called Step 1, in some detail.

Step 1 is undoubtedly the most important step in diagnosis, for if it is not done properly, the subsequent two steps of testing and inferring will not be performed correctly.

Step 1 is initiated when a patient presents to us with symptoms. The presentation, which usually includes patient’s age, sex, risk factors, symptoms is perceived as a problem which we seek to resolve by finding (diagnosing) the disease causing illness in this patient.

In general, a presentation does not provide us any significant evidence from which we could diagnose a disease with any confidence. Mostly, it functions as a clue which usually points towards several diseases, anyone of which could be the cause of illness in the patient.

It is customary in practice to suspect all these diseases, that is to initiate Step 1, and to list them to create a comprehensive differential diagnosis(2).

For some of the diseases in a differential diagnosis, the presentations from which we suspect them may be typical, which means that most patients with one of these presentations would have the respective disease.

And for some of these diseases, the presentations may be atypical, which means only few patients with one of these presentations would have the respective disease.

It is apparent that the typicality or atypicality of a suspected disease does not represent evidence for or against this disease in a given patient. It merely reflects the population from which the suspected disease has been drawn, the disease for which the presentation is typical has been drawn from a population having many patients with the disease and the disease for which the presentation is atypical has been drawn from a population having few patients with the disease.
Therefore, we suggest, typicality or atypicality represents the chance of a disease being present in a given patient and not evidence for or against it in this patient.

Therefore all suspected diseases in a differential diagnosis are diagnostic hypotheses without any prior evidence for or against them. Thus all suspected diseases in a differential diagnosis are on an equal footing as diagnostic hypotheses regardless of whether their presentations are typical or atypical.

This feature of a differential diagnosis is the key reason, we believe, that diseases with atypical presentations are diagnosed accurately in practice. This is seen most clearly in diagnostic exercises in real patients, such as clinicopathologic conferences (CPCs) and clinical problem solving exercises which are published regularly in the New England Journal of Medicine (3,4). An accurate diagnosis was made in 49 out of 50 CPCs due to creation such differential diagnosis in one study (3).

We believe, the creation of a comprehensive differential diagnosis in which all suspected diseases are diagnostic hypotheses without any prior evidence for or against them is a major factor in the high diagnostic accuracy of 85 to 90 percent in practice at large (5).

However, diagnostic errors due to failure to suspect a disease with an atypical presentation have been reported in several studies (6,7) which we believe is due to lack of experience about wide variation in presentations of a disease in different patients. It has been suggested that this experience could be provided to novice physicians in a virtual manner by having them review presentations of a given disease, pulmonary embolism for example, in 50 to 100 consecutive patients seen at a large medical center (8).

We suggest the only role of typicality or atypicality of a presentation is in prioritizing the testing of various suspected diseases in a differential diagnosis. The disease with the most typical presentation is tested first in a non-urgent diagnostic situation as it has the greatest chance of being present in a patient.

We note in the above description of suspecting a disease (Step 1) in diagnosis in practice that there appears to be no need for the Bayesian notion of prior
probability as prior evidence. A high degree of diagnostic accuracy of 85 to 90 percent in practice at large (5) and of 98 percent in CPCs (3) is achieved without this notion.

This notion would only be employed by us in diagnosis in practice, we suggest, only if it increased diagnostic accuracy to more than 90 percent. But we find employment of this notion would have the opposite effect, it would increase diagnostic errors in some patients by encouraging failure to suspect a disease with an atypical presentation by interpreting its low prior probability as evidence against it in a patient.

Therefore Bayesian reasoning of which this notion is a key feature is not employed in diagnosis in practice despite having been prescribed for over 50 years.

When we look closely at why Bayesian reasoning was prescribed in diagnosis in the early 1960s, we find the prescription was not made because Bayesian reasoning would increase diagnostic accuracy but because it is rational, with rationality being defined as not losing a bet in the long run if we look upon a probabilistic (Bayesian) diagnosis as a bet (9).

But for physicians in practice, diagnosing is not betting, our goal in diagnosis is diagnostic accuracy in every individual patient which is not possible in principle, we believe, if we adopt the Bayesian notion of prior probability as prior evidence in suspecting a disease.

We find it surprising, Bayesian reasoning with its notion of prior probability as prior evidence has continued to be prescribed for diagnosis despite lack of any evidence that it increases diagnostic accuracy.

This may be due to the widespread mistaken notion, as Sir Ronald Fisher pointed out many years back, that evidence for a hypothesis can only be represented by its probability (10). As he points out, it is better represented by its likelihood (ratio) and not by its probability (10).
It was specifically his unhappiness with the notion of prior probability of a hypothesis as prior evidence for it in Bayesian reasoning which led him to develop frequentist reasoning in which prior probability does not represent prior evidence for a hypothesis (11).

At present there is a fierce controversy (almost a war) between the Bayesian and frequentist camps in statistics about which method is better for inference. This controversy has been superbly described by Deborah Mayo in her recent excellent book ‘Statistical inference as severe testing: How to get beyond the statistics wars’ (11).

We as physicians do not need to get involved in these statistics wars. We just need to examine which of these two methods helps us achieve our goal in diagnosis of diagnostic accuracy in every individual patient regardless of prior probability of a disease and adopt (and prescribe) that method for diagnosis in practice.

On examination of these two methods, we find it is the frequentist method which helps achieve our goal of diagnostic accuracy in every patient which is the reason, we believe, it is employed during diagnosis in practice (12). In this method, a suspected disease is a diagnostic hypothesis without any prior evidence for or against it regardless of its prior probability (presentation).

References

1. Jain BP. Comment about diagnosis as a 3 step process posted on Discussion Board, Society to Improve Diagnosis in Medicine, Nov. 19, 2019.