Ibn Sina's *Canon of Medicine*: 11th century rules for assessing the effects of drugs

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In his Al Hammadi Lecture at the Royal College of Physicians of Edinburgh, John Urquhart,[1] professor of biopharmaceutical sciences at the University of California at San Francisco, contrasted Ibn Sina's *Canon of Medicine* (c. 1012) with Osler's *Principles and Practice of Medicine*.[2] Urquhart asked himself which of the two books he would want if he was marooned and in need of a guide for practical medicine. He opted for Ibn Sina's *Canon* because the book presents an integrated view of surgery and medicine. Ibn Sina tells his readers, for example, how to judge the margin of healthy tissue to remove with an amputation.[a] In contrast, Osler shunned intervention in his *Principles and Practice of Medicine*. The enduring respect in the 21st century for a book written a millennium earlier is testimony to Ibn Sina's achievement.

Abu Ali al-Husayn ibn Abd Allah ibn Sina (known as Avicenna in Europe) was born about 980 CE (370 H), near Bukhara, where his family moved soon after his birth.[3] Bukhara had been for centuries the glory of the Persian Empire, but the empire was falling apart into smaller kingdoms under the pressure of Arab invasions. This was one of the reasons that Ibn Sina had to move several times during his life. Despite this, he managed to write several outstanding books, which went on to influence the concepts and principles of scholars for centuries.

Ibn Sina's studies began in Bukhara under the guidance of several well-known scholars of the time, for example, Abu Abd Allah al-Natili. He studied logic, philosophy, metaphysics and natural sciences, and gradually developed an interest in medicine. His knowledge soon began to exceed that of his teachers. Ibn Sina began writing his major medical composition, *Kitab al-Qanun fi al-tibb* (*Canon of Medicine*), in Jorjan (also written as Gorgan) at the southeast corner of the Caspian Sea, and continued its composition in Rayy, an important medieval city south of modern Tehran, where two other great medical writers in Arabic, al-Razi and Ibn Hindu, were born.[4,5] The *Canon* was completed in Hamadan even further southwest, where Ibn Sina died in 1037 CE (428 H). Ibn Sina had intended to include his clinical case-notes in the book, but the paper on which they were written was lost before he was able to do so.[6]

The most celebrated medical book prior to the publication of Ibn Sina's *Canon* was the *Complete Book of the Medical Art* (*Kitab Kamil al-sinaàh al-tibbiyyah*) composed about 983 by Ali ibn al-Abbas al-Majusi. Although the Syrian physician Ibn al-Ibri (known as Bar Hebraeus), who died in 1286, judged this book to include more practical clinical advice than the *Canon*, he records that publication of the latter soon eclipsed memory of the former.[7] Indeed, Ibn Sina's *Canon* remained the most popular medical textbook in the world over the subsequent six centuries.[8]

Ibn Sina divided his *Canon of Medicine* into five books.[9] The first book – the only one to have been translated into English[10,11] – concerns basic medical and physiological principles as well as anatomy, regimen and general therapeutic procedures. The second book is on medical substances, arranged alphabetically, following an essay on their general properties. The third book concerns the diagnosis and treatment of diseases specific to one part of the body, while the fourth covers conditions not specific to one bodily part, such as poisonous bites and obesity. The final, fifth, book is a formulary of compound remedies.

The images of Ibn Sina's text shown in *The James Lind Library* are taken from an edition of his book published in Rome in 1593, part of the historic collection of the Sibbald Library of the Royal College of Physicians of Edinburgh. This version of

the book was based on a Florentine manuscript, and it is the first medical work to have been printed in Arabic. One of us (AT) translated the passages quoted from the Arabic text.

> *'Medicine is a science from which one learns the conditions of the human body with regard to health and the absence of health, the aim being to protect health when it exists and restore it when absent.'*

Then, after that famous opening sentence, Ibn Sina continues:

> *'Someone might say to us that medicine is divided into theoretical and practical parts and that, by calling it a science, we have considered it as being all theoretical. To this we respond by saying that some arts and philosophy have theoretical and practical parts, and medicine, too, has its theoretical and practical parts. The division into theoretical and practical parts differs from case to case, but we need not discuss these divisions in disciplines other than medicine. If it is said that some parts of medicine are theoretical and other parts are practical, this does not mean that one part teaches medicine and the other puts it into practice – as many researchers in this subject believe. One should be aware that the intention is something else: it is that both parts of medicine are science, but one part is the science dealing with the principles of medicine, and the other with how to put those principles into practice.'*

Ibn Sina begins the second book (on simple drugs, or *materia medica*) with a discussion on the nature and quality of drugs (they were each assigned a pair of qualities, cold or warm, dry or moist), and the way that mixing them influences their effectiveness. The second chapter (*maqalah*) of Book 2 is 'On knowledge of the potency of drugs through experimentation (*tajribah*)'.

> *'You can tell the potency of drugs in two ways, by analogy* (qiyas) *and by experiment* (tajribah). *We say experimenting leads to knowledge of the potency of a medicine with certainty after taking into consideration certain conditions.'*

Ibn Sina then specifies seven rules that need to be taken into account:

> *'1. The drug must be free from any acquired quality: this can occur if the drug is exposed to temporary heat or cold, if there is a change in the essence of the drug, or if the drug is in close proximity to another substance. Water, although cold by nature, will give warmth as long as it is heated; euphorbium, although hot by nature, will have a cold effect when cold; almond, although naturally neutral, will have a strong effect of heat if it turns rancid; and fish, although cold, is a strong source of heat if salt is added to it.*
> *2. The experiment must be done on a single, not a composite, condition. In the latter case, if the condition consists of two opposite diseases and the drug is tried and found beneficial in both, we cannot infer the real cause of the cure. Example: if we treat a patient suffering from phlegmatic fever with agaric and the fever abates, this does not mean that because it was useful for a hot illness agaric possesses the property of coldness. It is possible that the drug was effective because it dissolved the phlegm or removed it; when the [phlegm] disappeared the fever disappeared. This action represents both the direct and the accidental benefit of the drug. The direct benefit relates to the [phlegm], and the indirect refers to the fever.'*

Ibn Sina makes clear here that he realizes that if a patient suffering from more than one disease recovers after receiving a drug, one cannot infer that the treatment was the reason for the recovery. A treatment should be tested in a controlled environment to reduce confounding factors, in this case, by excluding patients with complex, multiple illnesses.

In the third rule, Ibn Sina stresses that a drug can affect the disease itself directly, and thus cure it, but that it can also have a secondary, accidental effect, and that it would then cure a symptom only, without removing the cause of the problem.

> *'3. The drug must be tested on two contrary conditions. If it is effective on both, we cannot judge which condition benefited directly from the drug. It is possible that the drug acted directly against one disease, and acted against the symptom of the other. Scammony, if used to treat a cold disease, would no doubt have a warming effect and bring benefit. If we try it on a hot disease, such as diurnal fever, it would also have a beneficial effect because it gets rid of yellow bile. In these cases, an experiment would be of no help in deciding whether [the drug] is hot or cold, unless we could know that it acted directly on one disease and acted on a symptom of the other.*

4. The potency of the drug should be equal to the strength of the disease. If some of the drugs are inadequate with regard to heat when compared to the coldness of an illness, they will not be able to effect a cure. Sometimes during their application against coldness, their function for producing warmth is weakened. So it is best to experiment first using the weakest [dosage] and then increase it gradually until you know the potency of the drug, leaving no room for doubt.

5. One should consider the time needed for the drug to take effect. If the drug has an immediate effect, this shows that it has acted against the disease itself. If its initial effect is contrary to what comes later, or if there is no initial effect at first and the effect shows up later, this leads to uncertainty and confusion. Actions in such cases could be accidental: their effect is hidden at first and later comes into the open. The confusion and uncertainty relate to the potency of the drug.

6. The effect of the drug should be the same in all cases or, at least, in most. If that is not the case, the effect is then accidental, because things that occur naturally are always or mostly consistent.

7. Experiments should be carried out on the human body. If the experiment is carried out on the bodies of [other animals] it is possible that it might fail for two reasons: the medicine might be hot compared to the human body and be cold compared to the lion's body or the horse's body … The second reason is that the quality of the medicine might mean that it would affect the human body differently from the animal body …

… These are the rules that must be observed in finding out the potency of medicines through experimentation. Take note!'

However closely one may identify modern notions about testing drugs in each of Ibn Sina's seven points, his seventh point remains very relevant. One of the few systematic comparisons of drug studies done in animals and humans showed substantial discordance, which the authors of the study attributed either to bias or to the failure of animal models to mimic clinical disease adequately.[12,13]

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Additional notes

[a]Professor Urquhart has kindly provided the following details: The book I have is entitled 'The Canon of Medicine' by Avicenna (Abu Ali al-Husayn ibn Abd Allah ibn Sina), adapted by Laleh Bahktiar. It is one in a series of Great Books of the Islamic World, © 1999 to Laleh Bahktiar. The ISBN number is: 1-871031-67-2. It is listed as being distributed by KAZI Publications, Inc., 3023 W. Belmont Ave, Chicago, IL 60618, USA. Their email is kazibooks@kazi.org.

The section in question is part of 'Lecture 24: On Making Incisions'. The first section, 24.1 is entitled General Remarks. The second section, on page 536, is entitled '24.2. Gangrene Excision'. In the 2nd paragraph of that section, numbered 2272, he writes: 'When you are about to excise the gangrenous part, cut along the bones where the flesh is adherent, and still healthy, and the pain is greatest, this being the indication of the healthy margin. Any part that is flabby belongs to the gangrenous part and must be excised with it.' The last sentence in the succeeding paragraph, #2273, states: 'The object is to separate the diseased part and its fasciae from the healthy tissue as far as possible, after which it can be wholly excised'. Then in the last paragraph, #2274, he writes: 'If the part affected is large, and with nerves, arteries and veins in the vicinity (for instance, the thighbone), and if the gangrenous change is very great, the doctor should leave the case severely alone'.