bin assignments of some genes. We ultimately plan to use the semiquantitative actionability scores to set a threshold for Bin 1, and we anticipate exploring different weighting systems for the key components of clinical actionability and/or thresholds to define Bin 1 in different clinical contexts. Thus, one could set a very high threshold such that Bin 1 contains very few genes, leaving more genes in Bin 2 for individualized decision making. One could also imagine using the continuum of actionability scores to facilitate individual decision making regarding return of results. It will be fascinating to hear more about the Tailored Result Selection Tool system, and we very much look forward to the results and lessons learned.

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doi:10.1038/gim.2013.25

Avicenna's view on medical genetics

The chief landmark in the history of genetics is most likely the work of Gregor Mendel on pea plants in the 19th century, which later was translated to the concept of Mendelian inheritance in medical genetics.[1] However, early theories of inheritance were described by Hippocrates (460–377 BC) and Aristotle (384–322 BC), and their observations formed the basis of the study of inheritance by the principles of science.[2]

Islamic medieval physicians also pointed out the hereditary nature of some disorders such as hemophilia, noted by Albucasis (936–1013 AD).[3]

We studied Avicenna's (Persian physician, 980–1037 AD) views on different aspects of medical genetics by reviewing his *Canon of Medicine*[4] and searched MEDLINE for relevant hereditary and congenital concepts and descriptions of temperament. We also investigated *Zakhireh-kharazmshahi* by Gorgani (a Persian physician inspired by Avicenna, 1041–1136 AD),[5] which is a comprehensive source in traditional medicine.

Three main topics in the *Canon*, including temperament (*Mizaj*) and its uniqueness in each individual, hereditary and congenital disorders and their classification, and the rationalization for inborn malformations, foreshadow the development of the field of medical genetics. Considering the significance of temperament in traditional medicine, Avicenna emphasized the individuality of people based on their unique temperament, which would later correspond to the unique genetic makeup of each person and presage the central notion of interindividual variation so critical to the work of Darwin.[2] In addition, Avicenna discussed the congenital versus acquired nature of some disorders such as hearing loss and muscle problems in his book and, in some instances, described their severity and differences in more detail.[4] In discussing the transmission of diseases from person to person, he named six conditions, including premature baldness, under the category of hereditary transmissions.[6]

Avicenna also classified congenital malformations into four categories: errors in form (such as broad head), errors in passages (such as stricture of the trachea), errors in cavities (cavities of the heart, for instance), and errors of surfaces (roughness and smoothness) (**Table 1**).[4]

On the cause of deformities, he explained that some come into play from the beginning because of a defect in the formative

Table 1 Avicenna's classification of congenital malformations into four categories: errors in form, errors in passages, errors in cavities, and errors of surfaces

Group	Subvarieties	Examples
Errors in form: here the form is changed from its natural grace to an extent that impairs its utility	Deviation from a natural straightness, straightness of a naturally curved line, squareness where there should be roundness, rotundity where there should be squareness	Head broad and round, with ossified sutures to an extent hindering mental power, curved shinbones, genu valgum, clubfoot, pupils congenitally elongated or slit-like or small, great rotundity of abdomen
Errors in passages	Too wide, too narrow, occlusion	Wide pupils, varices, aneurysms, the dilated blood vessels in pannus, small pupils, narrowed eyes, stricture of trachea or bronchi, stricture of esophagus, occlusion of venous orifices
Errors in cavities	Too large (distended), too small (contracted), obstructed and overfull, emptied	Distended scrotum, contracted stomach, contracted cerebral ventricles in epilepsy, obstruction in cerebral ventricles in apoplexy, cardiac cavities emptied of blood by reason of excessive joy or extreme pain
Errors of surfaces	The normal roughness replaced by smoothness, the normal smoothness becomes rough	At the orifice of the stomach, trachea, fauces

power of the sperm, and others come into force later in life, namely, in parturition, during the act of traversing the maternal passages, or in infancy.[6]

Gorgani also believed that no two persons were identical in their temperament, but there were similarities between the people of the same ethnic group. It is interesting to mention that, in *Zakhireh-kharazmshahi*, he speculated on how the "temperament" of the parent's germ cells could affect the gender of the fetus.[5]

Although Avicenna and others were, of course, unaware of genes as the units of inheritance, they nevertheless glimpsed a rough understanding of the hereditary and congenital nature of some disorders based on their careful observations. In addition, contribution of germ cells and environmental factors were explored in their speculations regarding the pathogenesis of congenital malformations. Because traditional medicine at that time was based on the concept of temperament, it was used to explain the differences between people affected by diseases and their response to treatments. Millenia later, modern medicine now finds itself finally understanding these differences through the rigorous and empirically validated concepts of genetics and epigenetics. Avicenna's precise classification of congenital malformations and speculations on intrapopulation differences highlight the quality of his scientific thinking and presaged critical concepts in modern genetics. In light of the inchoate theories formulated so long ago by Avicenna with the understandably crude models of that era, it is of interest to speculate what hints of future concepts are just now being glimpsed by today's geneticists. Surely, mysteries remain to be explained that will make future generations smile at our own naiveté.

ACKNOWLEDGMENT

The corresponding author dedicates this letter to Anita Rauch, who introduced him to the field of medical genetics.

DISCLOSURE

The authors declare no conflict of interest.

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doi:10.1038/gim.2013.27