Letters

High Priority Scores

Daniel E. Koshland, Jr.'s, editorial "Modest proposals for the granting system" (19 July, p. 231) states that the generally higher priority scores assigned to National Institutes of Health (NIH) grants are due to "grade inflation" and that this phenomenon has compressed many applications into the same priority range. This, in turn, has led administrators to superimpose their own systems for deciding how to allocate grant resources. He argues that peer review panels should return to "realistic evaluations" in order to discourage the manipulation of priority scores by administrators.

Koshland is correct about the problem, but I do not believe it is primarily due to priority score inflation. Study sections, as a collective body, do assign realistic priority scores. Except in occasional instances, they have not departed from what most feel are realistic evaluations. The problem is that the quality of grant applications is plainly higher than it was 15 years ago. Many promising and well-trained investigators have been produced by and now populate the system. It is inevitable that this causes an increase in the average priority scores because those scores are earned. I would even suggest that, for a given priority score, the quality today is higher.

The most serious problem is that the compression of scores has given administrators a rationale to discount them and to weigh heavily other considerations in their decisions as to who obtains funding. It is no longer true that there simply is a priority score cut-off or "pay-time" for funding, although this is still widely believed. The prize does not necessarily go to the fastest or the best. Among other factors, as Koshland points out, investigators with lower scores may get funded over those who have earned higher scores but who have other funding (even if it is for a different project). In what academic institution could we tell students who earned A's that they were to receive B's because they had earned A's in other courses, and worse, that their A was to be assigned to a student who earned a B? This is what is happening at NIH today.

The system bred an army of excellent investigators who now earn higher priority scores. I believe that the past success came by no-nonsense emphasis on quality as defined by the grading of grant applications by study sections. In those days, an A was an A. Everybody understood that funding lines had to be drawn somewhere and then adhered to. When you missed the funding line by a point, you missed. But you could aim and try again because the target was defined and not subject to manipulation. The danger today is not from the clustering of high priority grant applications with similar scores. The danger is that well-intentioned administrators, in the face of a difficult challenge, assume more and more power in the allocation of resources. And that, in the end, we forsake the rigorous standards and straightforward dealing which breeds success.

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Antimalarial Etymology

In his article "*Qinghaosu* (Artemisinin): An antimalaria drug from China" (31 May, p. 1049), Daniel L. Klayman provides a brief historical introduction in which he refers to the earlier use of an antimalarial natural product, the bark of the cinchona tree (from which the alkaloid quinine was subsequently isolated in 1834). He then goes on to discuss the recently isolated antimalarial drug artemisinin, derived from the herb *Artemisia annua*. Perhaps of interest, although not mentioned in Klayman's review, is the fact that the cinchona tree (and the genus *Cinchona*) is named in recognition of the contribution to the progress of medical science made by the Countess of Cinchón (or Chinchón), a member of the Spanish nobility who lived in Peru during the 1600's and who was instrumental in bringing this natural medicinal material to the attention of Europe (*1*, *2*).

Coincidentally, the genus *Artemisia* is named in honor of Artemisia of Caria, a noted woman botanist, medical researcher, and scholar who lived around 400 B.C. in southwestern Anatolia, in present-day Turkey (*1*, *3*).

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3. *The New Encyclopedia Britannica* (Encyclopedia Britannica, Chicago, ed. 15, 1974).

The derivation of the names of the genera *Cinchona* and *Artemisia* has provoked much interest and speculation. But, alas, there is hardly enough agreement on Herzenberg's version of the contribution to medical science by the Countess of Chinchón to warrant giving her a secure place in the malaria chemotherapy hall of fame.

The legend of the Countess takes several forms, the oldest having originated in 1663 with the Italian historian Sebastian Bado (*1*). According to his account, the first European to learn about "quina bark" (*quinaquina* in Quechuan means "bark of barks") was the Jesuit missionary Juan López. The bark, which came to be known as Peruvian bark, Jesuit bark, and *Cascarilla de Chahuarguera*, was used to cure the Spanish Corregidor of the city of Loxa of his intermittent fevers. In 1638, the Corregidor, having heard about the fevers of Doña Francisca Enriques de Ribera (*2*), the 39-year-old Condesa de Chinchón, wife of the Viceroy of Peru, Luis Geronimo Fernández de Cabrera y Bobadilla, Conde de Chinchón IV, sent her some bark and directions for its use. Under the guidance of the Condesa's physician, Juan de Vega, she drank an infusion of the bark and was cured rapidly of her tertian fever (*vivax* malaria). Two years later, the Conde and the Condesa, on their return to Spain, included a considerable amount of the wondrous bark with their baggage. This new cure was dispensed by the Condesa to the malaria-afflicted subjects of her husband's realm centered around Chinchón (about 24 miles southeast of Madrid). Because she spread the word of its therapeutic properties, it became known as the Countess' Powder (*Polvo de la Condesa, Pulvis Commitissae*). Kentish (*3*) relates essentially the same story but says the bark was brought back to Europe in 1649 by Cardinal Juan de Lugo, and its powdered form (*Pulvis Jesuiticum*) was sold there for its weight in gold.

According to Markham (*4*), Linnaeus named the genus which yields the febrifugic bark *Cinchona* (1742 edition) and *Cinhona* (1767 edition) in honor of the Condesa, whom he had only heard about and whose name he misspelled. Another version says that Linnaeus read about the Condesa in Bado's work. Bado's chief informant regarding the "quina" bark was an Italian merchant living in Peru, Antonio Bollus. Apparently, Bollus, in his correspondence with Bado, spelled the family name of the viceroy "Cinchón" so as to ensure its correct pronunciation in the Italian language (*5*). In any case, Linnaeus died before the incorrect spelling could be pointed out to him.

The legend of the Condesa was accepted as fact as recently as 1930 (*6*). However, the detailed diary of the Conde de Chinchón IV, kept by his secretary Juan Antonio Suardo, was published in 1936 and cast doubt on the accuracy of the Condesa's purported role. Historian Paz Soldan (*7*), on reviewing the *Diario*, expressed his belief that the true story was told by Suardo. The *Diario* tells that the Conde, rather than the Condesa, had malaria in 1638. The Condesa nursed the Conde back to good health using the "quina" or "precious unknown substance" that she obtained from Juan de Vega. The Conde recovered in 1640 and, in gratitude, built a temple to the Lady of Prado, to whom the Condesa had been directing her prayers. On their way back to Spain in 1641, the Condesa died in Cartagena (Colombia), and the Conde returned to Spain alone. Paz Soldan believes that it was not the Conde, but the Jesuit missionaries, who brought the bark to Europe. They were anxious to inform the public of its therapeutic properties, but encountered opposition to its acceptance. The Countess' Powder story was then concocted to romanticize its history and break down resistance to the new remedy.

Finally, another variant of the story (*8*) has the Conde suffering and recovering from malaria without ever being given the Peruvian bark. The Condesa then dies from an epidemic raging in Panama while she and the Conde await passage home. The Conde continues the journey home and apparently brings large quantities of the bark back to Spain, where it is then distributed by him and the Jesuits. How the Conde learned about the therapeutic powers of the bark remains unclear.

Recent evidence, therefore, makes it appear unlikely that the Condesa de Chinchón ever had malaria, ever partook of cinchona bark, or ever brought it back to Spain.

Herzenberg's second point, happily, is less controversial. Artemisia, the Turkish woman botanist, seems indeed to have been the inspiration for the genus bearing her name and is said to have "adopted" the herb mugwort (*Artemisia vulgaris*) as her own (*9*). She was probably named after Artemis, the complex feminist Greek goddess. Incidentally, Artemisia, in her guise as Queen of Caria, is also known for having built a large tomb, the Mausoleum, for her deceased husband, King Mausolus, in the city of Halicarnassus.

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References and Notes

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Photoreceptor Alignment

Mechanisms that could potentially underlie the precise alignment of cone photoreceptors with the center of the pupil have been proposed and evaluated since the directional sensitivity of the retina was first described (*1*). On the basis of a series of psychophysical studies, we proposed a positive phototropic mechanism for this phenomenon whereby photoreceptors are actively positioned toward the center of the light distribution in the pupil. Moving the light distribution (with a decentered aperture contact lens) led to a corresponding movement in the peak of the Stiles-Crawford function (*2*). As we reported, removing all light (with long-term monocular patching) led to a decrease in the peakedness of the function, that is, pronounced flattening (*3*). It now appears that our interpretation of the latter finding was in error. Recent measurements after monocular occlusion have failed to reproduce the flattening in the Stiles-Crawford function (*4*). It appears that the patching regime in the original studies was extreme and led to corneal edema, which itself can have a profound effect on the shape of the measured Stiles-Crawford function. Thus we wish to retract our original interpretation of the patching experiments. While an active light-driven alignment mechanism clearly plays a key role under normal lighting conditions, we have yet to identify mechanisms responsible for maintaining alignment in total darkness.

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Neogene Congo Basin Rain Forest

From reactions I have received concerning the article by Roger Lewin about the Bophuthatswana workshop on paleoclimates (Research News, 15 Mar., p. 1325), it could appear that I produced concrete proof for Neogene changes in the extent of the Congo Basin rain forest on the basis of plant and pollen records. This is, however, not the case.

In my lecture at the workshop I presented paleoenvironmental maps of various Late Cenozoic periods on the basis of oceanic and terrestrial evidence. The possible changes in the extent of the rain forest have been inferred from circumstantial evidence. The results of Caratini and Giresse (*1*) on the reduction of the Congo rain forest 18,000 years ago show that extrapolations I made for preparing of my maps may well be acceptable.

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