Reviewer's report

Title: Ultimate Answers in Medical and Health Profession Courses

Version: 3 Date: 1 March 2005

Reviewer: Randolph Nesse

Reviewer's report:

General

-------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Some of the below revisions may require a response, but I do not see a need for further review and think the author's can use the below suggestions as they see fit.

-------------------------------------------------------------------------------

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

This revision reads well and offers a provocative and interesting take on a new kind of thinking in medicine. The organization now orients the reader more promptly and the writing has been tightened. It seems likely that this article will, as intended, stimulate wide and productive debate.

I offer a few additional thoughts in hopes that they might forestall unnecessary criticism. The why questions posed by Darwinian or Evolutionary medicine have been around for a long time, what is new is trying to take them seriously. Thus, any opportunity to show how hypotheses can be tested should be taken up, and all interesting speculations should be labeled as such in order to avoid criticism by those who think that science is based only on experimental methods.

The opening example of childbirth now works well. This topic is covered at some length in Wenda Trevathan’s book “Evolutionary Medicine” and this offers a nice opportunity to refer readers to that work.

Page 6, I certainly agree that having a large brain seems advantageous, but if that is so, the question arises why hasn’t selection shaped big brains for lots of species. To be practical in making revisions, I would just tone this down a bit instead of getting into all the arguments about brain evolution.

Rounding of the pelvis is mentioned repeatedly, but isn’t it the size of the opening that matters most? I can remember my anatomy well enough to be helpful here, but other readers may have the same question.

The sickle cell section now works well, but the references are mostly either to general books or very specific articles. Much has been written specifically about selection for sickle cell and some of this literature should be cited. It is mentioned that the map of sickle cell disease and malarial prevalence in Africa are nearly the same, but not emphasized that this was the data that led Livingston and
others to argue for the evolutionary explanation. As for the Mediterranean, wasn’t malaria a problem there as well until recent years?

Bottom of page 7, would it more correct to say the sickle cell allele instead of the sickle cell gene?

Balancing selection is well described, but just adding a bit about how BOTH heterozygote phenotypes have lower RS than the average person with one copy of each allele would make the whole example a bit more clear.

Page 9 after the very first word individuals would the Weatherall article provide documentation for this assertion?

41% of individuals having hematological disorders seems high. Do the authors mean that 41% have an allele which, if homozygous, could cause disease?

The diarrhea example offers a chance to note how many important simple experiments have yet to be done. Instead of accepting as fact the assertions listed, the authors could in a sentence or two say how we could find out what is true.

Likewise, the authors seem to endorse the speculation that high rates of certain diseases in Ashkenazi Jews are because of protection against typhus or tuberculosis, but this is quite a controversial topic. There is no need to try to solve it here, but it is best to not assert what cannot be backed up.

The same goes for PKU. I think it was Diamond who speculated about this and about the HLA that predisposes to diabetes, but has anyone ever followed up? It would be better to point out how silly it is that years have passed with no one doing the work to find out.

Page 12, does leptin really for sure lead to a vicious circle? If so that is dramatic, but do qualify the assertion if it is not widely supported.

Insect data on senescence are dramatic for semelparity but readers won’t understand this. Rose’s studies of flower beetles are accessible and show how selection in the lab can increase life span at the cost of reproductive success.

Humans are one of the few species were there is an end to reproduction, and it is only for one sex; this is very rare in other species. is usually phrased as and few would attribute most aging to it and the calcium example from Williams remains, sadly, unstudied and only a hypothesis and fine possible example. Sapolsky and Finch have a recent article on evolution and Alzheimer’s disease that is very germane. Likewise I think there is a new article on evolution of hemochromatosis as resulting from selection for low iron to protect against infection, perhaps by Daniel Fessler.

I should be clear that I think this article is nearly ready to go, and the above suggestions should not delay publication. However, in only a few hours of editing the authors can better help readers to understand both the enormous potential of Darwinian medicine, and the challenges that arise when one tries to address such questions. Testing them is difficult and uses different kinds of evidence and different kinds of tests than most scientists are familiar with. If this is acknowledged, and if the emphasis is on how much exciting science needs now to be done to test these hypotheses, many will be inspired by this article to move the field further.
Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests