

Hello,

It is another month and another set of issues to be debated here, I think, with our busy schedules and demands placed on our time from every side, nobody will be able to go through all the research papers line by line. And I must confess that I am also not able to go through these articles through and through, but I have skimmed over these articles and fished out what I thought was important and might have practice implications.

There is a beautiful review article in current NEJM on thalassaemia, as this disease remains quite common, it would be worthwhile going through this paper, I have reproduced a full-page picture showing common complications and therapies of this disease on page 2

"Everything that exists in the universe is the result of chance and necessity" (Democritus, 460–370 BC), this holds true for antimicrobial drug resistance. But unfortunately, it is extremely difficult to think like a bacterium. In other words, predicting the emergence of resistance to a drug class by a precise molecular mechanism is nearly impossible (e.g., glycopeptide resistance in enterococci or plasmid-mediated resistance to fluoroquinolones). This paper from "Emerging Infectious Diseases" is difficult to understand; but it is for that time, when we are feeling fresh and feel like taking up something intellectually stimulating. Complete article at <http://www.cdc.gov/ncidod/eid/vol11no10/05-1014.htm>, abstract on page 3.

In defence of H. pylori? When all the world seem bent on eradicating it? Yes Sir, there is this editorial from Indian Journal of Medical Research, that tells about good things that this bacterium accomplishes. Check out some details on Page 4.

Then the last thing that caught attention this month was another editorial discussing the reference ranges. It analyzed the way we use reference ranges, told how it impacts clinical decision making and warned about mistakes that can be made if incorrect comparisons are made. Thought provoking editorial .. that one. (Page 5)

Any way these are some of the things that I thought worth bringing to your attention. I hope, they are worthy of a glance or two from you ;)

May I say that, would you mind, sending positive or negative comments about utility or futility of this newsletter to me at 9823244033 or drss.kale@gmail.com.

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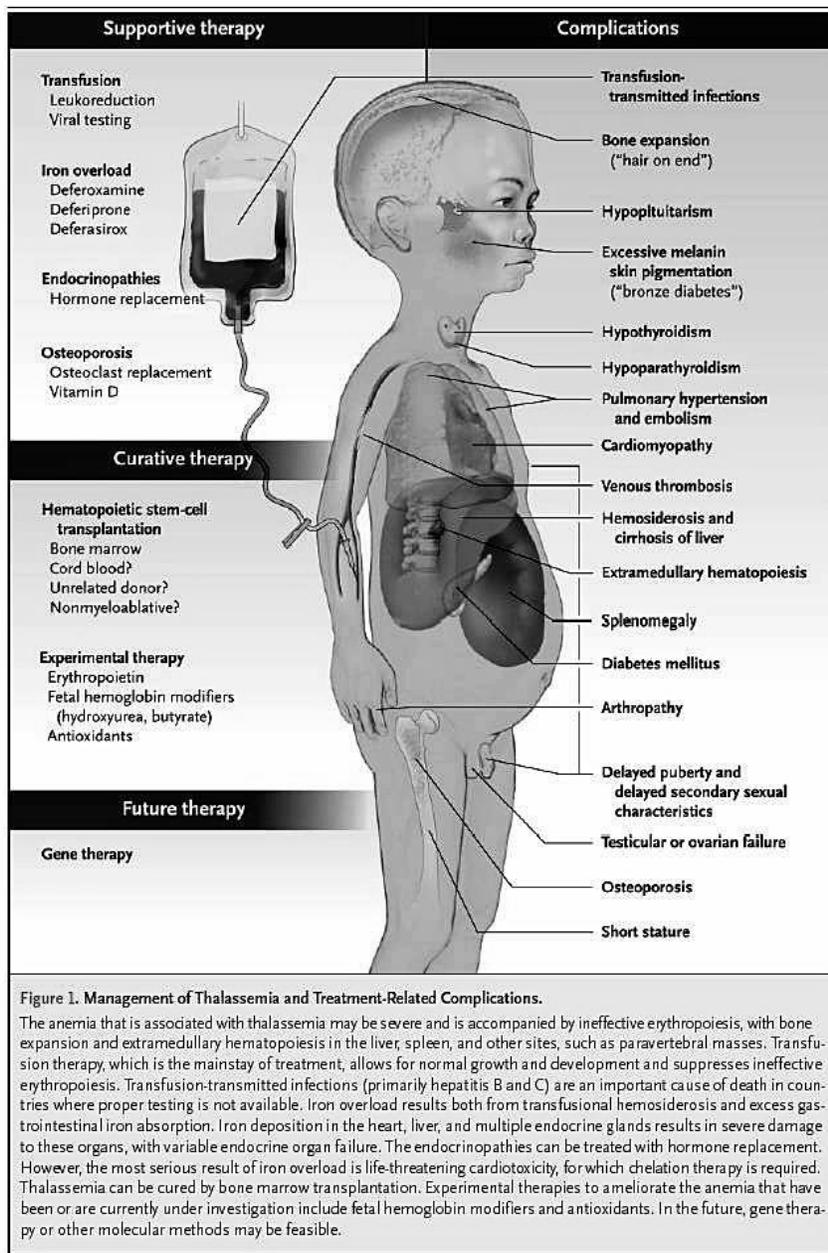


Figure 1. Management of Thalassemia and Treatment-Related Complications.
 The anemia that is associated with thalassemia may be severe and is accompanied by ineffective erythropoiesis, with bone expansion and extramedullary hematopoiesis in the liver, spleen, and other sites, such as paravertebral masses. Transfusion therapy, which is the mainstay of treatment, allows for normal growth and development and suppresses ineffective erythropoiesis. Transfusion-transmitted infections (primarily hepatitis B and C) are an important cause of death in countries where proper testing is not available. Iron overload results both from transfusional hemosiderosis and excess gastrointestinal iron absorption. Iron deposition in the heart, liver, and multiple endocrine glands results in severe damage to these organs, with variable endocrine organ failure. The endocrinopathies can be treated with hormone replacement. However, the most serious result of iron overload is life-threatening cardiotoxicity, for which chelation therapy is required. Thalassemia can be cured by bone marrow transplantation. Experimental therapies to ameliorate the anemia that have been or are currently under investigation include fetal hemoglobin modifiers and antioxidants. In the future, gene therapy or other molecular methods may be feasible.

It is easy to lie with statistics, but it's a lot easier to lie without them.
 – Richard J. Herrnstein

(Cont, 2)

The endangered gastric pathogen *Helicobacter pylori*: To eradicate or not?

Unfortunately, however, the *H. pylori* infection is in sharp decline in the western world. This may sound good news to many gastroenterologists around the world, but many argue that having a *H. pylori* colonization may be advantageous for the gut.

It has been shown that *H. pylori* produces cecropin-like peptide (antibacterial peptide) with high antimicrobial properties⁵.

Another study revealed that children infected with *H. pylori* were less likely to have diarrhoea than children without an infection, implying that *H. pylori* may be beneficial to human hosts.

Interestingly, there has been a marked decline in the instances of peptic ulcer disease and gastric cancer in the 20th century.

Concurrent with this is a dramatic increase in the incidences of gastrooesophageal reflux disease (GERD), Barrett's oesophagus and adenocarcinoma of the oesophagus in western countries⁷.

This observation led to the speculation that *H. pylori* may in some way be associated with these diseases and perhaps capable of preventing their onset.

Few people think more than two or three times a year; I have made an international reputation for myself by thinking once or twice a week.

- George Bernard Shaw

Those are my principles, and if you don't like them... well, I have others.

- Groucho Marx

(Cont, 3)

Perspective

Antimicrobial Drug Resistance: "Prediction Is Very Difficult, Especially about the Future"¹

Patrice Courvalin* *Institut Pasteur, Paris, France

Evolution of bacteria towards resistance to antimicrobial drugs, including multidrug resistance, is unavoidable because it represents a particular aspect of the general evolution of bacteria that is unstoppable.

Therefore, the only means of dealing with this situation is to delay the emergence and subsequent dissemination of resistant bacteria or resistance genes.

Resistance to antimicrobial drugs in bacteria can result from mutations in housekeeping structural or regulatory genes.

Alternatively, resistance can result from the horizontal acquisition of foreign genetic information.

The 2 phenomena are not mutually exclusive and can be associated in the emergence and more efficient spread of resistance. This review discusses the predictable future of the relationship between antimicrobial drugs and bacteria.

Table. Predictable resistance types

Organism	Resistance phenotype or mechanism
<i>Streptococcus pneumoniae</i>	Penicillinase, gentamicin, glycopeptides
<i>Streptococcus</i> groups A, C, G	Penicillins
<i>Listeria monocytogenes</i>	Penicillins, gentamicin
<i>Legionella pneumophila</i>	Macrolides, fluoroquinolones
<i>Salmonella enterica</i> serovar Typhi	Third-generation cephalosporins
<i>Haemophilus influenzae</i>	Third-generation cephalosporins
<i>Neisseria meningitidis</i>	Third-generation cephalosporins
<i>Brucella</i> spp.	Tetracyclines, rifampin, streptomycin
<i>Clostridium difficile</i>	Glycopeptides
<i>C. perfringens</i>	Penicillinase
<i>Chlamydia</i> spp.	Tetracyclines

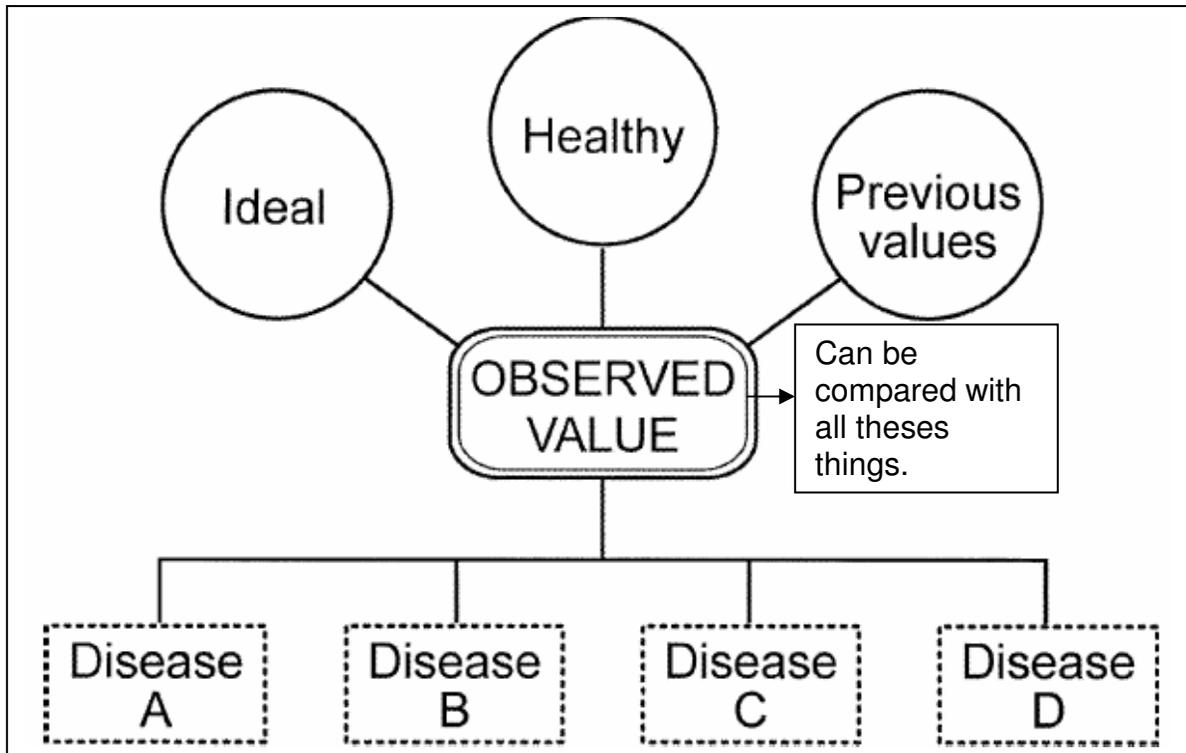
If you wish success in life, make perseverance your bosom friend, experience your wise counselor, caution your elder brother and hope your guardian genius.

Joseph Addison (1672 - 1719)

(Cont, 4)

Role of reference values in making medical decisions

Physicians make and analyze hundreds of clinical observations every day using patient histories, examination findings, radiographs, and lab data without thinking that every analysis involves reference comparisons. A simple example of the process is illustrated in the Fig.



This figure illustrates the variety of reference comparisons that might be made for a single observed value.

The most common comparison is with data based on healthy subjects. Other reference comparisons include comparisons to a variety of diseases, previous values, and values that convey risk (ideal comparison) even when they would pass the healthy subject comparison.

Your ability to make the correct diagnosis hinges on the accuracy of your observations and the reference comparisons you made. Failure at any step could lead to an error in diagnosis.

These illustrations make the point that our success in all medical decision making depends as much on selecting and properly using reference values and their limits - the boundaries that lead to changes in action - as it does on getting the measurements correct.

Improving the way reports display measured values, reference values, and their appropriate limits will reduce interpretative errors.

(End, 5)