ICMHA 2013 Keynote Speaker:

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Speech Title:
On A Mathematical Model of HCV

Abstract:

The speaker presents a mathematical model which describes the development of HCV (Hepatitis C virus), and its resistant variants, in a patient. One hundred and seventy million people are infected with HCV worldwide. In North America, more than five million people are supposed to be living with HCV. We assume that, apart from the variants that are already in the patient's blood stream, it requires only one more mutation at a specific neucleotide for an HCV virus to become resistant to the antiviral drug being administered, i.e. for u_0 (virus, together with all its variants, present when the treatment starts) to change into u_1, virus which is resistant to the drug (telaprevir). We assume that, in the presence of drug pressure, it is easier for u_0 to change to u_1 than the other way around, so that we assume that the probability of u_1 changing to u_0 is much smaller than the one of u_0 changing to u_1. We also assume that u_0 changes to u_1 after one more mutation at a given nucleotide. HCV has approximately 9600 nucleotides, and its copying mechanism is error prone at the rate of 1 in about 10,000. The virus lives for 2-3 hours outside a cell, so that new viruses are being produced inside the infected cells at about the same rate. The probability of its mutating at any **given** site in 8 replication cycles comes out to be 9.37031×10^{-8} and 1.04109×10^{-7} in 9 such cycles. We take this probability to be 10^{-7} which is the value of Q_1 in our model. We assume that the probability of u_0 changing to u_1 is Q_1 and that of u_1 changing to u_0 is $Q_2 = Q_1*Q_1$.

In a recent study, SVR rates in genotype 1 patients were highest in the peginterferon alfa-2a plus ribavirin arm, compared with the interferon alfa-2b plus ribavirin arm or the peginterferon alfa-2a alone arm.

The model correctly says that there are two possible outcomes of treatment of a chronically sick patient, either a rebound or SVR. It also points out the conditions under which each outcome will occur. It says that a rebound will occur if the "chronicity point" of the patient is in the basin of attraction of P_3, the equilibrium "rebound point" in our model. Treatment changes the location of the rebound point in our model and the rebound occurs if the drugs are not strong enough. However, even with a rather mild dose of a protease inhibitor, such a rebound may change to SVR. It should be noted that the behaviour of the virus in each case is triphasic. Such triphasic behaviour has been noted by other researchers.

About the Speaker:

Prof. B. D. Aggarwala is Professor Emeritus, Department of Mathematics and Statistics, University of Calgary. He has taught Mathematics at McGill University in Montreal, and then at the University of Calgary, Calgary, Canada since 1960. He served for two years as the Chairman of the Division of Applied Mathematics here at the University of Calgary and as chairman, he designed both the undergraduate and the graduate curriculum in Applied Mathematics. Numerical solutions of Ordinary and Partial Differential Equations being one of my areas of expertise, Prof. Aggarwala has considerable experience with the Mathematical Software called 'Mathematica'. He has published more than seventy research papers in the area of Applied Mathematics and Engineering. Currently his interests are in mathematical modeling for HIV/AIDS epidemiology.