432a Evaluation of Leukemia Patient Non-Compliance during Maintenance Chemotherapy: a Population Balance Model of Rbc Maturation

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Over the years, the discovery of new drugs as well as the understanding of existing drugs and their combinations has led to vast improvements in chemotherapy protocols. The success rates of the chemotherapy treatments for children with acute lympoblastic leukemia are quite good as 95% of the patients will enter remission. After initial, intensive radiation and/or chemotherapy treatments, a patient may remain on a prescribed maintenance regimen of chemotherapy for up to two years. During this period, only 85% of the patients remain in remission. Some of the resulting failures are attributed to the fact that many patients do not follow the maintenance regimen. Physicians have long known that many patients are delinquent with their maintenance chemotherapy; but with the improvements in treatment regimens, the fraction of deaths resulting from non-compliance is becoming more significant. Because of this, a simple, inexpensive diagnostic assay for monitoring patient compliance is needed. The mean corpuscular volume (MCV) of red blood cells (RBCs) has been investigated as a potential compliance indicator for several drugs such as azathioprine. The metabolites of azathioprine are purine biosynthesis antagonists leading to a decrease in the synthesis rate of DNA which slows down cell division and produces macrocytotic cells due to the resulting biomass accumulation. The net effect is a shift towards larger MCVs. As the MCV is already analyzed for a standard blood sample, no additional tests would be needed for compliance evaluation. However, the inter-patient variability in MCV shifts makes quantitative assessment of compliance difficult. This work investigates how these inter-patient differences may arise from the underlying developmental processes that lead to the corpuscular volume of a red blood cell. Specifically, a population balance model is written that describes the dynamics of the DNA, RNA, and biomass distributions in the bone marrow for each generation of red blood cells as they mature from colony-forming units (CFUs) to periphery ready mature reticulocytes. The response of the system to various medication scenarios will be used to evaluate patient compliance with the model assuming different efficiencies in the drug metabolism for different patients.