A Model for the Regulation of Mammalian Platelet Production[a]

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The pathophysiology of cyclical thrombocytopenia and idiopathic thrombocytopenia purpura are examined in a simple model for the regulation of mammalian platelet production. We let $P(t)$ denote the total number of platelets of all ages, T_m stand for the maturation time of a megakaryocyte, T_s represent the age of death (due to senescence) of a platelet, and γ be the (age-independent) random destruction of platelets. Then it may be shown that

$$\frac{dP}{dt}(t) = -\gamma P(t) + \beta(P(t - T_m)) - \beta(P(t - T_m - T_s))e^{-\gamma T_s} \qquad (1)$$

where $\beta(P) = \beta_0\theta^n P/(\theta^n + P^n)$ reflects the thrombopoietin feedback influencing the influx of cells into the recognizable megakaryocyte compartment, and n, θ, and β_0 are parameters. Equation 1 has the trivial steady state $P^* = 0$ for all values of the parameters. When $\beta_0 > \gamma/(1 - e^{-\gamma T_s})$, a second, non-trivial, steady state $P^* > 0$ appears, and the trivial solution is locally asymptotically unstable. Normally, $T_s = 10$ days and $T_m = 9$ days. We have used published clinical data[1] to determine the parameters n, θ, and β_0 in the feedback function $\beta(P)$. Using these, we numerically integrated Equation 1 for different values of the parameter γ. In FIGURE 1, the non-trivial steady state has lost its stability. Subsequent bifurcations led to irregular time series, an example of which is shown in FIGURE 2. Other simulations have revealed a wide range of possible behavior for Equation 1 as γ is varied, including low, sustained platelet levels, and oscillating nonperiodic counts similar to those observed clinically.[2]

[a]Supported by the Natural Sciences and Engineering Research Council of Canada (Canada) and the Fonds pour la Formation de Chercheurs et l'Aide a la Recherche (Québec).

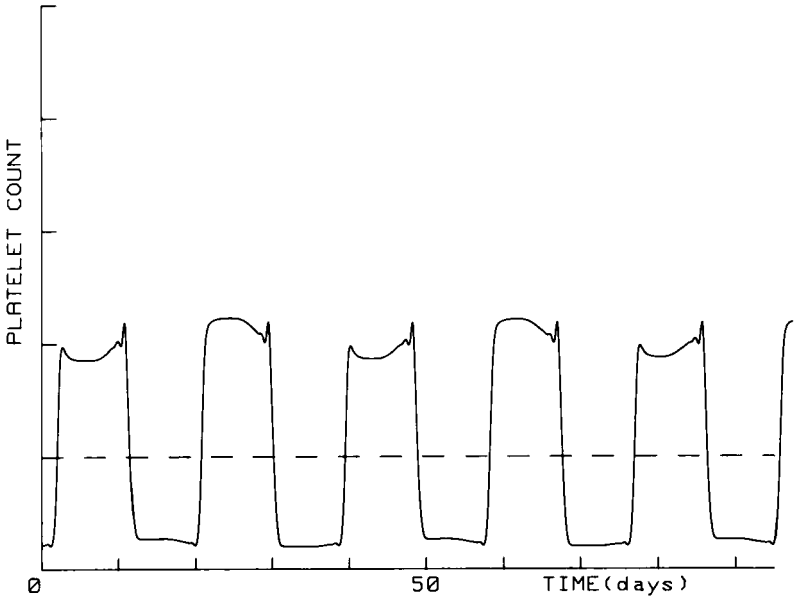

FIGURE 1. Platelet count as a function of time. Values of the parameters are n = 2.2, θ = .04, and γ = 3. The dashed line indicates one-tenth of the normal level.[2]

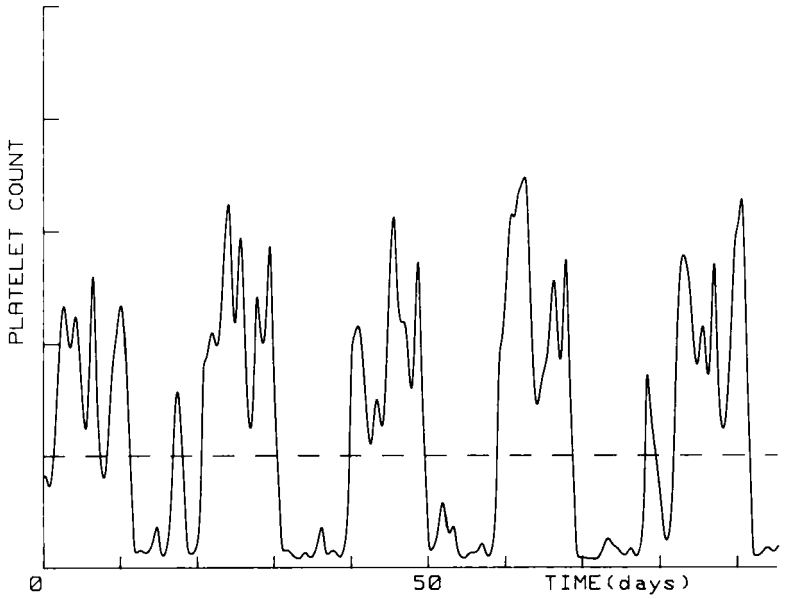

FIGURE 2. As in FIGURE 1, except γ is now 2.

REFERENCES

1. BRANEHOG, I., J. KUTTI & A. WEINFELD. 1974. Brit. J. Haematol. **27:** 127–143.
2. COHEN, T. & D. P. COONEY. 1974. Scand. J. Haematol **12:** 9–17.