Haematol 1981; 27:374–380.
4. Toghill PJ. Red cell pooling in enlarged spleens. *Br J Haematol* 1964; 10:347–357.
5. Peters AM, Saverymuttu SH, Bell RN, Lavender JP. The kinetics of short lived In-111 radiolabelled platelets. *Scand J Haematol* 1985; 34:137–145.
6. Peters AM, Walport MJ, Bell RN, Lavender JP. Methods of measuring splenic blood flow and platelet transit time with In-111-labelled platelets. *J Nucl Med* 1984; 25:86–90.

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REPLY: We very much appreciate the willingness of Peters and Myers to discuss our analysis (*1*) of splenic dynamics of radiolabeled platelets in idiopathic thrombocytopenic purpura (ITP). Before responding to the specific issues raised in their letter, we would like to comment briefly on general aspects of using mathematical models for describing biologic systems. It must be remembered that models are only a means to provide a better understanding of biologic mechanisms and should, therefore, not be classified as being strictly "right" or "wrong." The usefulness of a selected model is determined by its universality, i.e., its applicability to various pathophysiologic conditions. This does not mean that it is unjustified to use a model applicable only to a particular condition, e.g., the use of a closed two-compartmental model for the study of the dynamics of normal platelets. It was with these considerations in mind that we suggested the use of biexponential curve fitting instead of a closed two-compartmental model for analyzing splenic dynamics in ITP.

Our data may not totally invalidate the two-compartmental model in ITP. In fact, we observed a monoexponential time-activity course in 4 out of 33 ITP patients. We have not made any reference to a possible 'runoff' component due to platelet destruction because we have not as yet addressed this possibility by appropriate experiments, and are not fully convinced that data obtained from studying the splenic uptake of heat-damaged red cells can be applied to the kinetics of ^{111}In-labeled platelets. Peters and Myers correctly point out that our blood-pool curve is also biexponential and that this indicates the use of a three-compartmental model. The observation that there was no correlation between the exponential components of the blood-pool curve and that of the splenic curve is by no means meaningless. On the contrary, the lack of correlation strongly implies that the system contains other important components. However, in a closed two-compartmental system the blood-pool and splenic curves can be assumed to be complementary. In a forthcoming paper, we have compared the two- and three-compartmental models with each other and have shown the superiority of the latter in providing meaningful information on the effects of platelet autoantibodies on splenic dynamics.

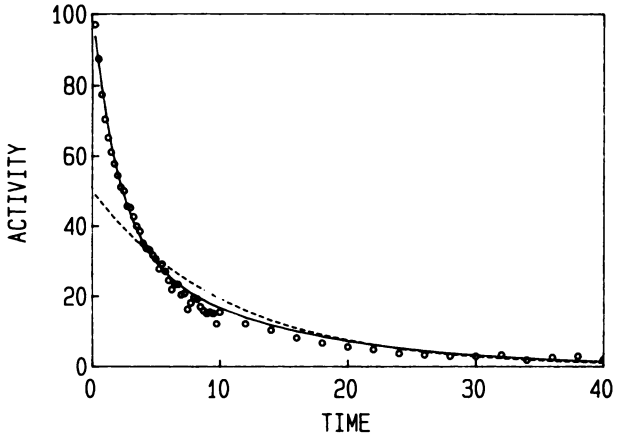

FIGURE 1
Inverted splenic time-activity curve observed after injection of ^{111}In-labeled platelets (circles) and fitting of biexponential (solid line) and monoexponential (dashed line) functions to the data.

It is true that the curve fitting procedure is very dependent on the residual function detection and that there are rare ITP patients in whom a splenic plateau value has not been reached after 40 min, but this does not preclude fitting a two-exponential function to the observed curve in these cases. It is our experience that a 40-min imaging time is sufficient for reliable data analysis and prolongation of the imaging time does not give additional information (most of our patients were imaged for 60 min).

We have now performed a statistical comparison of biexponential and monoexponential fits to the splenic time activity curves (Fig. 1) of each case studied. The goodness of each fit was calculated by reduced chi square test (*4*). The reduced chi square values of biexponential fits were significantly lower than the monoexponential ones ($p < 0.005$, two-tailed Student's t-test for paired samples), clearly demonstrating the biexponential nature of the function. In fact, in only three cases was the monoexponential fit superior to the biexponential one. In eight additional cases, the two fits were equally good but in the majority (22 cases) the biexponential was better.

According to Peters et al. (Ref. 3 page 143): "A potential error in deconvolution analysis is the assumption that the blood-pool signal recorded by the gamma camera is a true reflection of the arterial input into the spleen. This assumption would not be valid if some degree of platelet sequestration in the lungs or in the bone marrow of the chest wall, occurring during the course of dynamic imaging, was included in the blood-pool region of interest." Although these workers might now have changed their opinion concerning the usability of deconvolution analysis in platelet dynamics, we still share their earlier opinion with one essential amendment: deconvolution analysis under these methodologic circumstances is invalidated only if platelets taken up by extrasplenic sites are also partly released during the imaging period.

For the above reasons we are of the opinion that a closed two-compartmental model is not the best one for deriving information about splenic dynamics of short-lived platelets in ITP.

REFERENCES

1. Syrjälä MT, Savolainen S, Nieminen U, Gripenberg J, Liewendahl K, Ikkala E. Splenic dynamics of indium-111-labeled platelets in idiopathic thrombocytopenic purpura. *J Nucl Med* 1989; 30:1546–1549.
2. Bevington PR. Goodness of fit. In: *Data reduction and error analysis for the physical sciences.* New York: McGraw-Hill; 1969:187–195.

3. Peters AM, Saverymuttu SH, Bell RN, Lavender JP. The kinetics of short-lived indium-111 radiolabelled platelets. *Scand J Haematol* 1985; 34:137–145.

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The Effect of Carrier on Reaction Rates

TO THE EDITOR: The recent letter of Couch et al. (*1*) on the "Use of Carrier in the Preparation of Iodine-123 HEAT" represents a misconception concerning the role of carrier in radiotracer syntheses. Addition of carrier ^{127}I to a solution of ^{123}I does not increase the number or frequency of collisions between ^{123}I and the molecules to be labeled per se. The rate of the (radiochemical) reaction is not changed by this mechanism. It is true that the frequency of collisions between substrate and all iodine nuclides is increased but only those collisons between ^{123}I and substrate are pertinent to radiotracer formation. In any event an induced increase in the rate of a given reaction by some perturbation is not necessarily reflected in an increase in yield. The converse also holds—namely an observed increase in yield (as found by Couch et al.) does not require that the reaction took place more quickly.

In those cases where carrier has a favorable effect upon radiochemical yield, one must look elsewhere for reasons. Trace impurities present in the reaction medium, which are capable of consuming a significant proportion of the radionuclide or saturable adsorption sites on the walls of reaction vessels, syringes, etc. are among the many possibilities. Addition of carrier under these circumstances serves to increase the effective concentration of the radionuclide.

REFERENCE

1. Couch MW, Greer, DM, Thonoor CM, Williams CM. Use of carrier in the preparation of iodine-123 HEAT. [Letter]. *J Nucl Med* 1989; 30:1916–1917.

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REPLY: Dr. Wilson has apparently misconstrued our brief discussion of the higher yield of product in the carrier-added reaction. A more complete explanation is as follows: in addition to HEAT, $^{123}I^+$ ions also interact with impurity molecules in the reagents and with the walls of reaction vessels, etc. In a no-carrier-added reaction, these interactions utilize a significant proportion of the $^{123}I^+$ ions. When carrier is added, the large number of carrier ions added also partake in these undesirable "side reactions," leaving a larger number of $^{123}I^+$ ions available for reaction with HEAT. Thus there are, *effectively*, more collisions between $^{123}I^+$ and HEAT in the carrier-added reaction than in the no-carrier-added reaction and this results in a correspondingly higher yield of product.

It is certainly correct that neither the reaction rate nor the number of collisions between two species by themselves is altered by the addition of carrier. We did not state nor did we mean to imply the contrary.

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