Reprinted from TRANSFUSION, January-February 1983
Vol. 23, No. 1
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The impact of adenine and inventory utilization decisions on blood inventory management

M. A. COHEN, W. P. PIERSKALLA, AND R. J. SASSETTI

The use of citrate-phosphate-dextrose-adenine as an anticoagulant for whole blood increases the storage period permitted for whole blood and red cells from 21 to 35 days. A simulation model was used to analyze the possible consequences for outdates and shortages of the addition of adenine. The model accepts as input (1) the maximum age (21 or 35 days), (2) parameters describing the demand and supply distributions, and (3) parameters describing inventory control (crossmatch recycle period, transfusion fraction, deviation from optimal target inventory levels). These parameters were varied over wide ranges, and a full factorial design was carried out. The observed shortage and outdate rates were then related (via multiple regression) to the parameter values. The resulting shortage and outdate functions indicated the effect of parameter changes, including extending the lifetime from 21 to 35 days, and the joint effect of changing more than one parameter. Conclusions indicate that, while the contribution of an increased lifetime to reducing shortages and outdates can be substantial, this contribution can be easily dissipated by relaxing the tightness of other inventory management controls. **TRANSFUSION** 1983;23:54–58.

BLOOD BANKING includes a management process which has its origins in the development of anticoagulant solutions which permit the maintenance of blood in the liquid state outside the body. The use of sodium citrate as an anticoagulant opened the field of blood preservation by permitting the storage of blood for up to 1 week.[1,2] Since that time, there have been continuous efforts to increase the shelf life. The addition of adenine, a metabolite in the energy cycle of the red cell, to citrate-phosphate-dextrose maintains red cells in an acceptable state for at least 35 days. This represents an addition of 66 percent to the usable life of a unit of blood.

Outdating is a characteristic of blood logistics which has been accepted as inevitable but undesirable. However, the decision-making process relative to maintaining adequate blood inventory levels must take into consideration two essentially antithetical components: shortage and outdating. While it is possible to treat each of these factors with equal weight in selecting an inventory level, it is likely that, in most circumstances, the unit cost of shortages will significantly exceed that of outdates. Consequently, cost-minimizing inventory levels lead to a certain amount of outdating. Hence, the extension of shelf life is viewed as a cost-effective method of increasing the blood supply by reducing outdates.[3–5]

The selection of inventory levels is also influenced by such factors as the crossmatch recycle time, transfusion-to-crossmatch ratio, and issuing policy. Management policies other than inventory levels have also been applied to reduce outdating. For example, recycling of older blood from a hospital with low usage to one with high usage (effectively increasing the transfusion-to-crossmatch ratio) is associated with a decrease in outdating.[6]

Brodheim and Hirsch[7,8] speculated that with a given inventory level, increasing the shelf life to 35 days would permit reduction of shortage rates from 18 to 20 percent per year to 6 to 8 percent per year. They implied that this reduction results from decreased outdating. The experience of Kreuger et al.,[9] indicates an expected reduction in outdating of 50 percent or more.

It is possible, however, that with the extension of shelf life, other blood management policies might be relaxed, which could minimize or neutralize the benefits of the extended life in reducing outdates and/or shortages. It is the purpose of this paper to examine the effects of the increased life on outdating and shortage rates. We will also examine the effects of

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From the Department of Decision Sciences, Wharton School, and the Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, Pennsylvania, and the Rush-Presbyterian-St. Luke's Hospital Center, Chicago, Illinois.

This research was partially supported by PHS-HS000786 from the National Center for Health Services Research and by NSA - GK40034 from the National Science Foundation.

Received for publication April 2, 1981; revision received February 8, 1982, and accepted February 9, 1982.

0041-1132/83/0100/0054 $01.05 © J. B. Lippincott Company

variation in other management policies on the outcome.*

A simulation model was used to analyze the specific effects of management controls and environmental factors on shortages and outdates. We show that the determinants of the number of outdates and shortages in a particular period in a blood inventory are (1) the inventory levels by blood type, (2) the demand levels by blood type, (3) the mean age of blood supplied to the hospital, (4) the crossmatch release period, and (5) the transfusion to crossmatch ratio. When the shelf life of red cells is extended from 21 to 35 days and all of the above determinants are unchanged (i.e., maintained at their previous levels), then the shortages and outdates of red cells will drop. But, if some of the determinants, singly or together, are not controlled, then shortages and outdates will again rise, and the substantial benefits from adenine on the extension of shelf life will be lost.

Also in this paper we extend our earlier analysis[3] by presenting a simple decision rule for setting optimal target inventory levels by blood type under either a 21- or 35-day dating and for specific values for the various determinants mentioned above. In using this rule it is not necessary for the blood bank administrator to choose a shortage rate for system operation since the inventory level recommended by the rule reflects the optimal trade-off between shortages and outdates.

Methods

As in our previous studies,[3] demand data from Rush-Presbyterian-St. Luke's Medical Center, Evanston Hospital, and the North Suburban Blood Center in the metropolitan Chicago area were used. The methods of analyses involved various statistical estimation techniques, economic analysis, inventory operations analysis modeling, and simulation. The model specifies input factors relating to system environment and control policy. The factors considered in this analysis included parameters to specify the daily demand process, the age of units supplied, target inventory levels, the transfusion-to-crossmatch ratio, crossmatch release time, issuing policy, shortage cost, and outdate cost.

Model outputs include detailed records of all inventory transactions and the age distributions of both assigned (crossmatched) and unassigned inventories. These outputs are used to estimate the "optimal decision rule" i.e., the relationship between the cost-minimizing target inventory level, S, and the various factors. In a similar way, the outdate rate, O_R, and shortage rate, S_R, were determined by relating them to the various factors as well as the target inventory rule.

Results

The estimated decision rule for target inventory level is summarized in equation (1). Because of the added variable for the maximum shelf life (L is either 21 or 35 days), the coefficients of the decision rule (1) are slightly different than in our earlier work.[3] However, when one sets L = 21 in this equation and computes the optimal inventory level, the results round to the same optimal inventory numbers.

$$S = \frac{4.755(d_M)^{0.6964}(p)^{0.1146}(L)^{0.1332}}{(D)^{0.0453}} \qquad \text{Equation (1)}$$

where d_M is the mean daily demand for a blood type, p is the average transfusion to crossmatch ratio, D is the crossmatch release time in days, and L is the maximum shelf life in days.* All coefficients are significant at the 0.01 level or less and $r^2 = 0.99$.

The blood bank administrator can compute the optimal target inventory level for each blood type from equation (1) by inserting type-specific d_m, p, D, and L. A range of 2 to 50 units demanded per day (which corresponds to an annual volume of between 300 to 10,000 transfusions) was considered in the experimental design. Almost all blood banks have type-specific mean demand volumes which fall into these ranges, and hence equation (1) has wide applicability.

The small values of 0.1146 for the power of p, 0.1332 for the power of L, and 0.0453 for the power of D in equation (1) indicate that their influence on S is not nearly as large as that of d_M with its power of 0.6964. Taken singly over the respective ranges of each variable, with the others held constant, the effect of p, D, or L on S is, at most, 6 percent to 8 percent.

For fixed values of p, L, and D, a positive exponent of 0.6964 for mean daily demand in the optimal decision rule indicates that as the mean daily demand is increased, there is less than a proportional increase in the optimal order quantity. Alternatively, a blood bank which doubles its activity (in terms of mean daily demand) should increase its optimal inventory level by no more than 70 percent (provided that p, L, and D remain the same).

The initial effect of switching to a 35-day shelf life with d_M, P, and D unchanged, means that the optimal target inventory level, S, must be increased by 7 percent. This increase in S occurs because the increased shelf life permits more blood to be kept without loss due to outdating, while, at the same time, the larger inventory reduces the frequency of shortages.

The outdate rate is the ratio of the mean number of units outdated to the mean number of units transfused plus units

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*Throughout this paper we will use the definitions: *Demand*, the number of blood units of any one type that are set aside for possible transfusion (i.e., crossmatched) on a given day; *Shortage*, a situation in which the demand exceeds the number of units of blood in inventory; *Shortage rate*, the long-term fraction (or percentage) of days on which a shortage occurs; *Usage*, the number of blood units of any one type transfused on a given day; *Outdate*, a blood unit discarded because of exceeding the maximum age (21 days without adenine, and 35 days with adenine); *Outdate rate*, the ratio of mean number of blood units outdated to mean number of blood units transfused plus those outdated.

*The use of type and screen and maximal blood ordering policies will have the effect of bringing p close to a value of one and reduce the value of D. If p were to equal one, and/or if D become less than one, then the derived functions for S, O_R, and S_R would not be strictly valid and should be viewed as approximations. In such circumstances both p and D should be set to 1 to obtain the appropriate approximation.

Table 1. *Effect of Combining Various Management Policies*

						S_R*			O_R†		
						L			L		
Case	d_M	p	D	A	$\lvert S'-S \rvert$	21	35	% Decrease‡	21	35	% Decrease‡
1	2	0.5	1	1	1	4	2	50	0.1	0.0	100
2	2	0.5	1	5	1	11	6	45	1.7	0.4	76
3	2	0.5	1	10	2	19	11	42	5.0	1	80
4	2	0.25	1	5	1	15	8	43	9.7	2	79
5	2	0.25	4	5	1	16	9	40	24	5	79
6	2	0.25	1	10	2	26	15	42	29.3	6.3	78
7	2	0.25	4	10	2	28	16	43	73.1	15.6	79
8	20	0.5	1	1	1	2	1	50	0.1	0.1	100
9	20	0.5	1	5	1	5	3	40	0.2	0.1	100
10	20	0.5	1	10	8	25	14	44	0.7	0.1	86
11	20	0.25	1	5	1	7	4	43	1.3	0.3	77
12	20	0.25	4	5	1	7	4	43	3	0.7	77
13	20	0.25	1	10	8	33	19	42	4.0	0.9	78
14	20	0.25	4	10	8	36	20	44	10.0	2.0	80

*S_R expressed as shortage days per thousand days
†O_R expressed as percent
‡% decrease between value from L = 21 to L = 35

outdated, and the shortage rate is the fraction of days on which a shortage occurs. In establishing the relationship between the outdate rate and its causal variables, it was evident that one of these explanatory causal variables should be the deviation of the actual inventory level, S′, from the optimal inventory level, S. If $S' > S$, then the outdates should increase because more blood is on hand than needed; if $S' < S$, then the outdates should decrease. In each case the reverse holds for the effect on shortages.

We can hypothesize the effect of the other causal variables such as the crossmatch release time, D, and the mean age of units, A. As either increases, the outdates should increase. The reverse should hold for the variables d_M, p, and L. That is, the larger the mean demand, transfusion-to-crossmatch ratio, or the longer the maximum shelf life, the lower should be the outdates. The regression for O_R is given by

$$O_R = \frac{4.11052\,(D)^{0.66033}(A)^{1.57255}(e)^{0.00799(S'-S)}}{(d_M)^{0.8856}(p)^{2.54564}(L)^{3.01945}} \qquad \text{Equation (2)}$$

where e is the base of the natural logarithms.

From the regression results in equation (2), we can see that these expectations are true. All of the coefficients are significant at the 0.01 level or less and their algebraic signs agree with the above hypotheses. Furthermore, these variables explain 71 percent of the variation in the dependent variable. ($r^2 = 0.71$)

This regression function captures the effects of these six variables on the outdate rate. These same causal variables were used to explain the variation in the shortage rate, except that instead of the deviation (S′−S), the reverse deviation (S−S′) was used. Consequently, if $S' < S$, the shortage rate should increase because the actual inventory level S′ is below the optimal level; and if $S' > S$, the shortage rate should decrease. The other variables are expected to have the same effect on the shortage rate as they did on the outdate rate. As d_M, P, or L increase, the shortage rate should decrease. As D or A increase, the shortage rate should increase.

As shown in equation (3), these expectations have been realized. All of the coefficients are significant at the 0.01 level or less and are of the correct sign. The log/exponential-linear regression explains 59 percent of the variation in the dependent variable. ($r^2 = 0.59$)
The regression equation is

$$S_R = \frac{0.09629 \times (e)^{0.17356(S-S')}(A)^{0.57441}(D)^{0.05359}}{(d_M)^{0.34867}(L)^{1.09577}(p)^{0.43568}} \qquad \text{Equation (3)}$$

These relatively complex equations for O_R and S_R allow us to examine the impact of adenine on the outdate and shortage rates for blood. By changing L from 21 to 35 days and holding all of the other controllable variables S, p, D, and A constant, O_R decreases by 80 percent and S_R decreases by 43 percent.

Table 1 depicts a variety of cases which show the effect of combining various management policies with the change in shelf life. Cases 1 through 7 have a low mean daily demand and represent either rare blood types or blood banks in small hospitals. Cases 8 through 14 represent large mean daily demand and can represent common blood types or a large blood bank. D, p, A and $\lvert S'-S \rvert$ are allowed to vary to reflect different management policies.

The variations in p and D represent examples of internal management policies since p and D are affected by the working relationships between the blood bank and the ordering physicians. Variations in A and $\lvert S'-S \rvert$ represent external management since the age and amount of arriving blood at the hospital are often dependent upon the policies of a regional blood center. However, an increase in A may also represent the lengthening effect on shelf life due to the introduction of adenine. The resultant S_R and O_R are tabulated for both 21 and 35 day shelf lives and the percentage decrease in each is listed.

Cases 1 and 8 represent the unusual circumstances of an ideal, optimally managed hospital blood bank which draws all of the blood it uses (A = 1) and has good control over its donor scheduling so it can closely achieve its optimal target inventory levels ($|S' - S| = 1$). The transfusion-to-crossmatch ratio is 0.5, i.e., one transfusion for every two crossmatches; the crossmatch release time is 1 day, i.e., if not transfused, blood is released within 24 hours. For both the case of small mean demand (two units per day), or large, (20 units per day), the shortage and outdate rates are very small for either a 21-day or 35-day shelf life. Case 1 ($d_M = 2$) would experience a shortage rate reduction from 4 days per thousand to 2 days per thousand when going from 21 to 35 days' shelf life. The outdate rate is 0.1 percent for a 21-day life and less than 0.1 percent for a 35-day life. Similar statements hold for case 8.

Cases 2 and 9 represent a blood bank with a more realistic mean age of arriving blood, A = 5 days. There is a threefold increase in S_R and up to a fivefold increase in O_R over the ideal depicted above.

In cases 3 and 10 we can see a different phenomenon occurring. These data depict the case in which the internal management of the blood bank is extremely good, $p = 0.5$ and $D = 1$ day, but external management is not. The average age of the arriving blood, A, has increased to 10 days and the absolute deviation $|S' - S|$ has also increased to two units for case 3 and eight units for case 10. This situation would prevail in the case where the administrator depended on external sources of supply such as community blood centers which were either poorly managed or operated on a shipping policy of sending the oldest units first to the hospital blood bank. In this situation (case 3), with small d_M, there are 19 days of shortage per thousand with a 21-day life and 11 days shortage per thousand with a 35-day life. The outdate rates are 5 percent and 1 percent respectively. In case 10, the shortage rate was 25 days per thousand with a 21-day life and 14 days per thousand with a 35-day life.

This last example illustrates that good internal management (high p, low D) can compensate to some extent for the uncontrollable external factors of age or amount of blood supplied. The increase in maximum life from 21 to 35 days results in about a 50 percent drop in the shortage rate and an 80 percent drop in the outdate rate if all other conditions are held constant for either the small or large demand.

A more interesting picture develops as the quality of the internal management is allowed to deteriorate. Internal management becomes especially critical if external management is poor. Cases 4 and 11 depict the same situation as cases 2 and 9 except that the transfusion-to-crossmatch ratio is decreased 0.25, i.e., only one of every four units crossmatched is transfused. The crossmatch release time is still 1 day, all arriving units are fresh, and absolute deviation from optimal inventory is small. The shortage rate remains relatively small with either the 21-day or 35-day shelf life. However, the outdate rate rises significantly. Note that for these cases the rates are significantly higher than cases 2 and 9, i.e., a 30 percent rise in the shortage rate and 200 to 600 percent rise in the outdate rate.

If the internal management deteriorates further to $D =$ four days but the external management is good, i.e., $A = 5$ and $|S' - S| = 1$, then for both small and large demands the shortage rate does not change much in value but the outdate rate again changes significantly (see cases 5 and 12). In these cases, a dramatic effect on outdating by changing the shelf life from 21 to 35 days is seen. The additional 14 days of shelf life for each unit significantly compensates for the negative effect of the large crossmatch release time, $D = 4$.

In the case where the internal management is mixed, $p = 0.25$, and $D = 1$, but external management again is poor, $A = 10$ days and $|S' = S|$ is larger (cases 6 and 13). For both small and large demand there is a large increase in the shortage rate (a 6- to 19-fold increase in the number of days of shortage from the overall well-managed system of cases 1 and 8 and a 4- to 19-fold increase over the semi-well-managed system of cases 4 and 11). The outdate rate is also poor. Again, there is significant help from the increase from 21-day to 35-day life. Several conclusions can be drawn from this example. First, poor management of low demand blood banks causes very large outdating (29%). (This may be the case in rural or small transfusion services.) Second, poor management of large demand blood banks does not result in large outdating, i.e., there is a reasonably low outdate rate of 4 percent. Third, the effects of low $p = 0.25$ can be greatly reduced (by 75–80%) through the increase in maximum life to 35 days. Finally, in the situation where both the internal and external management are poor there is a synergistic effect (cases 7 and 14). The shortage rates are very poor and the outdate rates rise dramatically. In these cases the overall poor management of the blood resource leads to excessive shortages and significant outdates in the system even if the shelf life is extended.

A comparison of the "worst" cases (7 and 14) and the "best" cases (1 and 8) highlights our observations. "Good" internal and external management yields a 7- to 20-fold decrease in the shortage rates and an approximately 20- to 800-fold decrease in the outdate rates vis-a-vis "bad" internal and external management. The other cases illustrate intermediate levels.

Discussion

For purposes of determining the impact of an adenine additive on the shortages and outdates of blood at any blood bank, there is a complex interaction of many variables on the system. Some of these variables are under the control of the blood bank administrator and others are possibly under the control of external administrators such as community blood center directors. Significant reductions in shortages and outdates, however, can be made by a combination of "good" overall management and a 35-day maximum shelf life.

Specific conclusions can be made about the effects of the adenine additive and the effects of management. The addition of adenine is significant and beneficial for both shortages and outdates. With no change in the other variables the shortage rate will drop by about 43 percent. With no change in the other variables the outdate rate will drop by about 80 percent. This should ultimately lead to an 8 to 10 percent decrease in the number of donors necessary to maintain the same level of supply.

The effect of management can be viewed from the perspective of the sensitivity of shortage and outdate rates to each variable changed. With no change in the other variables a decrease in the transfusion to crossmatch ratio, p, from 0.5 to 0.25 will increase the shortage rate about 50 percent and the outdate rate about 450 percent. An increase in the crossmatch release time $D = 1$ day to $D = 4$ days will increase the shortage rate about 8 percent and the outdate rate about 150 percent. An increase in the average age of arriving blood from A = 5 to A = 10 days will increase the shortage rate about 50 percent and the outdate rate about 200 percent. An increase in the deviation below the target inventory from $(S - S') = 1$ to $(S - S') = 8$ will increase the shortage rate about 240 percent and decrease the outdate rate about 6 percent. An increase in the deviation above the target inventory from $(S' - S) = 1$ to $(S' - S) = 8$ will decrease the shortage rate about 80 percent and increase the outdate rate about 6 percent. Finally as noted above, the increase of shelf life from 21 to 35 days results in a decrease in outdates of 80 percent and a decrease in shortage rate of 43 percent.

To capture the full effects of the benefits from the addition of adenine, the other variables must not be allowed to deteriorate, i.e., p should not drop, D and A should not increase, and the actual inventory level S′ should be held close to the target inventory level S given by equation (1). However, because shortages and outdates will initially drop due to the addition of adenine, there may be tendencies to crossmatch more units than needed, to leave units on crossmatch longer, to obtain older blood on average from outside sources (this is inevitable if outside sources of blood do not change their inventory levels and management practices), or to allow large deviations from S. These should be resisted. It does not take much of a negative change in p, D, A, or $S - S'$ to lose all of the benefits of adenine.

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M.A. Cohen, Ph.D., Department of Decision Sciences, The Wharton School, University of Pennsylvania, Philadelphia, PA 19104.

W.P. Pierskalla, Ph.D., The Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, PA 19104. (Reprint requests)

R.J. Sassetti, M.D., Director, Blood Center, Rush-Presbyterian-St. Luke's Hospital Center, Chicago, IL 60612.