Uses and Limitations of Survival Studies of Erythrocytes Tagged with Cr\(^{51}\)

By Max M. Strumia, Lawrence Taylor, Albert B. Sample, Louise S. Colwell and Ann Dugan

INTRODUCTION

SINCE THE INTRODUCTION of the procedure for tagging erythrocytes with sodium chromate (Na\(_2\)Cr\(^{51}\)O\(_4\)) for the purpose of determining the volume of circulating red cells,\(^1\) \(^2\) \(^3\) considerable work has been done on the nature of the binding, the elution factor and the effect of chromium on red cells,\(^4\) \(^5\) resulting in the establishment of a practical technic for study of red cell survival.

The purpose of this report is to present our experience with Cr\(^{51}\) tagging of red cells and to point out certain essential limitations in the applications of the method to the study of hemolytic phenomena in vivo.

PROCEDURES

Sodium chromate tagging

Twenty-five ml of blood obtained by venipuncture are introduced by syringe into a sterile rubber stoppered 50 ml bottle containing 3.2 ml of the ACD anticoagulant. One-half to 1 ml of sterile sodium chromate solution\(^*\) containing approximately 500 microcuries of Cr\(^{51}\), as Na\(_2\)Cr\(^{51}\)O\(_4\), is diluted to a volume of 5 or 10 ml with 0.9 sodium chloride solution. A volume of this diluted sodium chromate containing approximately 60 microcuries is added to the blood with gentle but thorough mixing at room temperature. With this dose, the resulting concentration of chromium metal is between one and three micrograms per ml of blood, depending on the specific radioactivity. When survival studies are carried out on stored ACD blood, the calculated volume of Cr\(^{51}\) solution is mixed with 28 ml of blood.

The blood is equilibrated with the chromium in a 37 C. water bath for twenty minutes. We find that the maximum amount of Cr\(^{51}\) will be taken up by the erythrocytes within this period of time, but the uptake varies between 65 and 95 per cent of the amount available depending on the hematocrit of the blood, i.e., the higher the hematocrit, the larger the volume of red cells and the higher the Cr\(^{51}\) uptake, provided the volume of the sample of whole blood remains constant—in our case 25 ml.

At the end of the period of incubation, the blood is thoroughly mixed, and 10 ml are withdrawn into a 10 ml calibrated syringe and immediately injected into the recipient. At the same time a portion of the remaining chromated blood is centrifuged and the plasma is separated.

The uptake of Cr\(^{51}\) by the red cells is determined by the differential count on diluted samples of whole blood and plasma as follows: a 1:100 dilution of the remaining chromated blood and a 1:25 dilution of the separated plasma are made. Radioactivity measurements are carried out by counting gamma emission from 3 ml samples of the diluted material placed in a flat-bottomed test tube, using a well-type scintillation counter which has a thallium activated sodium iodide crystal. The activity of the cells is expressed as counts per min-

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*Abbott Laboratories, Oak Ridge, Tennessee.
†N. Wood Counter Laboratory, 5491 Blackstone Avenue, Chicago 15, Illinois.
**Table 1.**—Body Hematocrit: Venous Hematocrit in 11 Normal Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Dye plasma volume ml.</th>
<th>Cr(^{51}) red cell volume ml.</th>
<th>Body hematocrit</th>
<th>Venous hematocrit (^1)</th>
<th>Venous hematocrit (^2)</th>
<th>Body hematocrit (^1)</th>
<th>Body hematocrit (^2)</th>
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</thead>
<tbody>
<tr>
<td>E.B.</td>
<td>3158</td>
<td>2070</td>
<td>39.6</td>
<td>45.1</td>
<td>44.6</td>
<td>0.88</td>
<td>0.89</td>
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<td>H.F.</td>
<td>2903</td>
<td>2085</td>
<td>42.0</td>
<td>49.1</td>
<td>46.3</td>
<td>0.86</td>
<td>0.91</td>
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<td>E.P.</td>
<td>3035</td>
<td>2118</td>
<td>41.1</td>
<td>44.5</td>
<td>45.4</td>
<td>0.89</td>
<td>0.91</td>
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<td>H.C.</td>
<td>2980</td>
<td>2160</td>
<td>42.0</td>
<td>46.1</td>
<td>47.0</td>
<td>0.91</td>
<td>0.89</td>
</tr>
<tr>
<td>J.M.</td>
<td>3636</td>
<td>1850</td>
<td>37.9</td>
<td>44.5</td>
<td>43.2</td>
<td>0.85</td>
<td>0.88</td>
</tr>
<tr>
<td>R.M.</td>
<td>2623</td>
<td>2370</td>
<td>47.5</td>
<td>51.2</td>
<td>49.3</td>
<td>0.93</td>
<td>0.86</td>
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<tr>
<td>W.B.</td>
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<td>2184</td>
<td>40.2</td>
<td>45.6</td>
<td>45.9</td>
<td>0.88</td>
<td>0.88</td>
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<tr>
<td>R.G.</td>
<td>2971</td>
<td>2389</td>
<td>44.5</td>
<td>45.8</td>
<td>45.1</td>
<td>0.97</td>
<td>0.99</td>
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<tr>
<td>W.C.</td>
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<td>44.9</td>
<td>44.2</td>
<td>0.89</td>
<td>0.89</td>
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<tr>
<td>J.M.</td>
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<td>1930</td>
<td>44.9</td>
<td>47.7</td>
<td>46.9</td>
<td>0.94</td>
<td>0.96</td>
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<tr>
<td>D.P.</td>
<td>2371</td>
<td>1930</td>
<td>44.9</td>
<td>51.2</td>
<td>50.2</td>
<td>0.88</td>
<td>0.89</td>
</tr>
</tbody>
</table>

**Average**

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<tr>
<td></td>
<td></td>
<td></td>
<td>0.90</td>
<td></td>
<td>0.91</td>
<td></td>
<td></td>
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</tbody>
</table>

Venous hematocrit 1 is determined at 0 time; venous hematocrit 2 is done one hour after initiation of procedure, at which time approximately 60 ml. of blood have been removed and 10 ml. of chromated red cells have been injected.

**Determination of Erythrocytes Volume**

The blood volume of the patient is determined from the red cell volume as measured by the radioactive sodium chromate method or from the plasma volume as measured by the Evans blue method. When fresh normal red cells are transfused into a normal subject, the red cell volume is determined with the Cr\(^{51}\) dilution method according to the formula:

$$\text{Red cell volume} = \frac{\text{Total } \text{Cr}^{51} \text{ in transfused cells}}{\text{Cr}^{51} / \text{ml. of whole blood} \times \frac{100}{\text{hemtc}}}$$

In all other instances, i.e., when the red cells are not fresh or when the recipient is not a normal subject, the red cell volume is determined by the dye plasma volume and the venous hematocrit, as follows:

$$\text{Red cell volume} = \frac{\text{Plasma volume} \times 100}{100 - (0.91 \times \text{hemtc})} - \text{Plasma volume}$$

To check the validity of our procedures, the relation of venous hematocrit to total body hematocrit was determined in 11 normal subjects. The total circulating red cell volume was determined with the Cr\(^{51}\) method, and at the same time the plasma volume was determined by the Evans blue method. The body hematocrit was obtained as follows:

$$\text{Body hematocrit} = \frac{\text{Red cell mass (Cr}^{51})}{\text{Red cell mass (Cr}^{51}) + \text{Plasma volume (Dye)} \times 100}$$

Two determinations of the venous hematocrit were carried out, at 0 time and 1 hour after initiation of procedure, at which time approximately 60 ml. of blood had been removed for study of the dye plasma volume and 10 ml. of chromated cells had been injected.

* Not corrected for total body value.
The average ratio of the body hematocrit to the venous hematocrit was found to be 0.90 and 0.91 (see table). These values are well in accordance with those suggested by Gibson et al., Gray and Frank, and Chaplin, Mollison and Vetter. The determination of the hematocrit was carried out with the capillary high speed method with which we have evidence that the amount of plasma trapped in the erythrocyte column is negligible.

Survival Studies of Cr⁵¹ Tagged Red Cells

Samples of blood are collected from the patient at ten, twenty and thirty minute intervals post-transfusion and, on subsequent designated days, for a period of seven to ten days.

A hematocrit determination is carried out on the transfused blood and on each blood sample; the blood volume determination is repeated at the end of the sampling period in all recipients, except the normal individuals.

Samples are prepared on the day of collection and counted altogether at the end of the survival period, at which time the activity of the plasma of all collected samples is insignificant, and can be disregarded. When samples of blood collected within five days of transfusion are counted immediately, a correction is made for radioactivity of plasma, in addition to Cr⁵¹ decay. Correction for Cr⁵¹ decay is not made when collected blood specimens are counted at the end of the observation period with the sample of transfused blood. A suitable chromium standard is counted at the beginning and after every 10 measurements.

The 100 per cent survival of tagged cells is calculated as follows:

\[
100\% \text{ survival} = \frac{\text{Counts/minute in transfused cells}}{\text{Total red cell volume (ml.)}}
\]

and the apparent survival:

\[
\text{Apparent }\% \text{ survival} = \frac{\text{Counts/minute/ml. of whole blood} \times 100 \times 100}{100\% \text{ survival}}
\]

Fecal Urobilinogen and Hemolytic Index

The fecal urobilinogen was determined by the quantitative method of Watson using improvements subsequently suggested by Watson and his coworkers. Aliquots of mixed stools, accurately collected over 4-day periods, were analyzed and results calculated in terms of milligrams of urobilinogen per 24 hours. The stool collection period is obtained in hours, from the time the last stool is discarded to the time the last specimen is collected.

The total amount of hemoglobin in circulation is obtained from the total red cell volume, the venous hematocrit and the hemoglobin concentration as follows:

\[
\text{Total circulating hemoglobin} = \frac{\text{red cell volume}}{\text{hematocrit uncor.}} \times \text{Hb Gm./100 ml.}
\]

The hemolytic index is calculated from the above data as follows:

\[
\text{Hemolytic index} = \frac{\text{Daily fecal urobilinogen (mg.)} \times 100}{\text{Total circulating hemoglobin}}
\]

In a series of 10 normal individuals our values for the hemolytic index ranged from 9.1 to 28.8 and averaged 19.4.

RESULTS

1. Auto-transfusion in a normal individual or transfusion from a normal individual into a compatible normal recipient

A typical result of auto-transfusion of fresh Cr⁵¹ tagged blood in a normal individual is shown in figure 1. This procedure is currently employed by us to test factors involved in whole blood sterilization and red cell collection and stor-
age, with consistently satisfactory results. The possible effect of minor blood factors are thus avoided.

Similar results, which are shown in figure 2, were obtained when 8 compatible normal individuals received transfusions of fresh ACD blood from normal donors. This technic has been successfully employed to study the post-transfusion survival of red cells, both fresh and stored. We have found this method practical and reliable within a period of observation of 7 to 10 days. Our experience with longer periods is not sufficiently large to warrant an opinion. Figure 3 represents results of a typical observation.

In some of these individuals, contemporaneous determinations of post-transfusion red cell survival with the non-agglutinated cell method (Ashby method, O cells in A recipients) indicate a good agreement between the two technics, i.e., with an average survival of 80 per cent or better of Cr tagged fresh red cells at 8 days, a disappearance of transfused cells at 120 days or better is obtained with the Ashby method. Similar conclusions have been reached by Sutherland et al.

The types of cases so far discussed and illustrated represent examples of conditions where decline in radioactivity of samples of blood is a fair measure of survival of transfused red cells.

2. Transfusion of abnormal cells in a normal recipient

Transfusion of abnormal cells into a normal recipient is illustrated by two cases. The first patient, a 47-year old white man, suffering from a form of chronic acquired humoral hemolytic anemia, was observed during one of the relapses.

Fig. 1.—The cross-hatched band in all figures indicates the range of the apparent post-transfusion survival of fresh ACD red cells, Cr tagged.
SURVIVAL OF

SURVIVAL %
100

APPARENT POST-TRANSFUSION SURVIVAL RATE OF FRESH ACD RED CELLS, Na$_2$Cr$^{51}$O$_4$ TAGGED, IN 8 NORMAL HUMANS

DAYS POST-TRANSFUSION
0 1 2 3 4 5 6 7 8

0 1 2 3 4 5 6 7 8

APPARENT POST-TRANSFUSION SURVIVAL RATE OF FRESH ACD RED CELLS, Na$_2$Cr$^{51}$O$_4$ TAGGED, IN 8 NORMAL HUMANS

DAYS POST-TRANSFUSION
0 1 2 3 4 5 6 7 8

Fig. 2.—Apparent post-transfusion survival rate of fresh ACD red cells, Na$_2$Cr$^{51}$O$_4$ tagged, in 8 normal humans.

Fig. 3.—Transfusion of stored ACD blood in normal recipients.
The anti-human globulin test was positive, and the daily fecal urobilinogen output in this patient averaged 350 mg. per diem over a 12-day collection period. On the basis of an initial measured circulating hemoglobin of 216 Gm., the hemolytic index of 162 represented a very great increase over the normal. The patient’s red cells, presumably sensitized, were removed in the blood stream of a normal individual at a very fast rate for the first two days; thereafter, the remaining cells, or about 60 per cent of the transfused mass, probably not sensitized, disappeared from circulation at a normal rate (lower curve, fig. 4).

The practical application of this type of study on patients with hemolytic anemia is readily appreciated. As already stated, the decline in radioactivity per unit volume of cells closely represents the disappearance of the tagged transfused cells from circulation.

The second patient was a white woman of Southern Italian extraction, aged 31, suffering from a minor form of thalassemia, with extremely severe elliptocytosis, who was splenectomized approximately three years before the studies here reported were carried out.

Splenectomy considerably improved the patient’s condition. The hemolytic index was found to be variable but generally elevated (average 94), and Cr$^{41}$ survival studies were carried out by transfusing the patient’s cells into a normal individual and by reinjecting the cells into the patient herself. The results are
Studies of red cell survival were carried out by chromation of the patient's FMG. 5.—Upper Curve: Auto-transfusion of cells in a patient with extreme elliptocytosis. This patient had been splenectomized. Lower Curve: Transfusion of cells from the same patient into a normal individual.

shown in figure 5. About 35 per cent of the patient's cells transfused in a normal patient disappeared from circulation immediately. This was probably due to the rapid removal from circulation of the more highly deformed cells (cigar-shaped). The remaining cells disappeared at a nearly normal rate. The auto-transfusion indicated that the patient destroyed her own cells at a rate faster than normal but much more slowly than the rate of destruction by the normal recipient and more slowly than indicated by the hemolytic index. Apparently the normal recipient's spleen played an active part in removal of the more altered cells from circulation.

3. Auto-transfusion in a patient with abnormal red cell turnover

A white man, aged 67, later found to be suffering from monocytic leukemia, was admitted to the hospital for study after a series of 33 whole blood transfusions received over a period of 165 days, or approximately 40 ml. of packed red cells per diem.

On admission, the total blood volume was 4977 ml., with a red cell mass of 1040. The urobilinogen output was determined on a 4-day collection at 150 mg. per diem, indicating an excess in relation to the mass of red cells (hemolytic index 40).

Studies of red cell survival were carried out by chromation of the patient's
cells and auto-transfusion. The results are indicated in figure 6. It points apparently to a better than normal survival of the tagged cells in a patient with obvious hyperhemolysis. Repeated determinations of the patient’s red cell mass actually indicated, over a 7-day period, an average daily loss of 68 ml. of packed red cells, and a bone marrow biopsy revealed complete replacement of normal bone marrow by monocytic elements.

4. **Transfusion of normal cells in a recipient with accelerated red cell destruction**

The patient of acquired auto-immune hemolytic anemia illustrated under (2) above offers a good example of the possible error involved in the transfusion of normal red cells in a recipient with accelerated red cell destruction. Twenty ml. of fresh, normal compatible ACD blood were chromated and the red cells injected into the patient. Figure 4 (upper curve) indicates that apparently these cells disappeared from circulation at an accelerated rate. Actually during this period of observation the hemolytic phenomena decreased in intensity while the rate of red cell production remained high (10.6 reticulocytes per cent). Consequently the daily volume of newly produced cells exceeded the volume of destroyed cells and the circulating red cell mass increased. If a correction of about 10 per cent for this change is made, the disappearance of the normal transfused cells falls within the expected normal value. Proof that the normal cells were well retained was furnished by the fact that repeated transfusions caused in the patient the expected rise in the red cell volume.

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**Fig. 6.—Auto-transfusion of Cr⁵¹ cells in a patient with an accelerated destruction of the circulating red cells but greatly diminished production of new cells.**
DISCUSSION

In the studies reported here, the period of observation has been limited to 7–10 days. The reasons for this limitation are as follows: 1) Observation without treatment of patients with hyperhemolysis beyond these limits is not practical. 2) The transfusion of a single unit of blood into a number of recipients necessitates the use of relatively small units of blood, and the radioactivity measurements of these small samples cannot be carried out for too long periods of time. Larger volumes of transfused blood and consequently larger doses of Cr⁴¹ can be used when it appears desirable to prolong the observation period. This procedure is particularly useful in determining the effect on red blood cells of method of collection, storage, etc.

Limitation of the studies of survival of tagged red cells to periods of 7–10 days is desirable and satisfactory for clinical purposes; it is probable that minor variations in the survival rate could be missed with this reduced observation period.

Cr⁴¹ tagging has been applied to the study of survival of red cells under 4 conditions:

1. Blood from a normal individual may be tagged and immediately re-injected into the same subject, or blood obtained from a normal individual and stored for varying periods of time can be tagged with Cr⁴¹ and transfused into the donor himself or into normal compatible individuals. In either case, and accepting the fact that the normal recipient maintains a constant volume of red cells by replacement of new cells for those normally removed from circulation, the observed decline in radioactivity is due to: a) decay in radioactivity of Cr⁴¹, b) elution of chromium from tagged cells, and c) removal of obsolete tagged cells from the blood stream.

A correction is routinely made for radioactivity of plasma and decay of Cr⁴¹, but a correction is not generally made for elution, and simply the “apparent” rate of disappearance of chromated cells is reported. The results are generally noted as counts per minute per ml. of whole blood, corrected for hematocrit.

We have found this method of determination of post-transfusion red cell survival very satisfactory for the study of the effect of various factors on the red cells. Among the factors studied have been methods of collection, rate of cooling, surface of the receptacles employed, temperature of storage, agents used for sterilization, etc.

2. Red cells from a patient suspected of having abnormalities affecting the red cell life span may be tagged with Cr⁴¹ and immediately transfused into a normal recipient. Under these conditions, assuming as in (1) above a constant volume of red cells and a normal rate of replacement in the recipient, the measure of the decline in radioactivity per unit of red cell volume becomes a measurement of survival of the tagged, transfused patient’s cells in a normal recipient.

This method of determining the alterations of red cells by transfusing them in a normal recipient and studying the disappearance rate has been widely applied, using various techniques such as the Ashby method, N¹³ tagging, etc. The Cr⁴¹ method, because of its simplicity and more ready availability, is highly commendable for this purpose and, in our experience, has proved satisfactory.

3. Blood from patients having an altered turnover of red cells may be tagged with Cr⁴¹ and re-injected into the patient. In this manner, for statistical pur-
poses, the numerical changes in the tagged cells represent changes of the entire volume of red cells. Such patients generally have a hyperactive bone marrow, and respond to red cell losses with greatly accelerated production. In this condition radioactivity changes, measured per unit volume of red cells, are subject to one additional factor, besides the three mentioned under 1 above; this is dilution of the Cr⁴¹ tagged cells by the release into the blood stream of an unknown volume of new non-tagged red cells, assuming that they are destroyed at a rate lower than that at which they are released. This factor is not taken into consideration in the case of normal recipients (1 and 2 above) because the rate of release of new, non-tagged red cells may be considered as equal to the rate of removal of obsolete cells.

When the tagging of red cells with Cr⁴¹ is used as a means to determine the survival of red cells the formula more generally applied is one in which the apparent survival is calculated on the basis of radioactivity per unit of packed cells. Typical is the formula suggested by Ebaugh:

\[
\text{Percentage of donor cell survival} = \frac{\text{Radioactive Cr}^{41} \text{ per ml. of recipient's packed red blood cells}}{\text{Total erythrocyte (Cr}^{41} \text{ transfused) \times recipient total red cell mass}} \times 100
\]

The validity of this formula is based on the assumption that the volume of red cells remains constant from day to day, that is, the subject receiving the transfusion produces daily a volume of red cells equal to that which is destroyed. This is not always the case with patients suffering from hemolytic disorders, and it is essential to keep in mind that the variations in the radioactivity of samples reflect both loss of the tagged cells and new cell production.

Loss of cells by hemorrhage or hemolysis, without replacement and consequent dilution by newly produced cells, would not cause a change in radioactivity of the unit volume of tagged cells, since tagged cells and non-tagged cells are lost at a similar rate. Therefore, if, during the period of observation, the volume of newly produced cells is less than the volume destroyed, then the apparent survival for the period of time will be greater than the actual. This is well illustrated by the auto-transfusion in the 67 year old male suffering from monocytic leukemia with greatly reduced red cell production (fig. 6).

If, on the other hand, the rate of new red cell production exceeds the rate of red cell loss, then the decline of radioactivity per unit volume would indicate a rate of red cell loss in excess of the actual. This occurs often when the rate of hemolysis, after a hemolytic crisis, declines, while the rate of red cell output increases or remains high. This is illustrated by the transfusion of normal red cells in the patient of acquired auto-immune hemolytic anemia during a period of diminishing hemolytic phenomena with continued active hyper-regeneration (fig. 4).

The rate of loss of red cells under these circumstances can be evaluated only if the rate of new cell production or the total circulating red cell mass are known and an appropriate correction made. Direct measure of the red cell production is possible with radioactive Fe or N⁵ tagging, but either method is at least impractical under ordinary clinical conditions.

The determination of the daily fecal urobilinogen output may be used with
the measure of the mass of circulating blood for calculating the hemolytic index (Miller et al.) which reflects in an approximate quantitative manner the rate of red cell destruction.

Weinstein et al. reported a half life of red cells of one day in a patient suffering from idiopathic acquired hemolytic anemia. This rate of red cell destruction, while possible, appears somewhat difficult to explain but becomes more readily understood if at the time of the observation, the rate of new cell production exceeds the rate of red cell loss, thus producing an excessive dilution and apparent disappearance of the tagged cells.

4. Cells from a normal individual may be tagged with Cr51 and injected into the patient being studied.

Under this condition, as under 3 above, the rate of new cell production by the recipient is a factor affecting the volume of the red cell mass. Measures of the radioactivity per volume of red cells must be corrected for variations in the red cell mass, by carrying out measurements of the blood volume at intervals of time during the period of observation.

CONCLUSIONS

1. Auto-transfusion of Cr51 tagged red cells in a normal individual or transfusion of similarly tagged cells from a normal individual into a compatible normal recipient is a valid method for measurement of the post-transfusion survival of these cells. It is particularly useful in determining the effect of various factors in the collection and storage of blood used for transfusion.

2. Transfusion of Cr51 cells from a patient suspected of having abnormalities of the red cell, affecting their life span, into a normal recipient is a very satisfactory method for determining the existence of alterations of the red cells.

3. When auto-transfusion of Cr51 tagged red cells is used to determine the life span of red cells in a patient suffering from hemolytic phenomena, corrections of the values obtained must be made according to the variations in the volume of red cells caused by the rate of new red cell production. The validity of such corrections by repeated determinations of the circulating red cell mass is subject to the limitations of the accuracy of the method. Determinations of the volume of the red cell mass at the beginning and end of the observation, with frequent determinations of the hematocrit in the intervening days, appears to be a satisfactory procedure for clinical purposes.

The hemolytic index is generally in fair accord with results of Cr51 survival studies corrected for variations in the red cell mass.

CONCLUSIONES IN INTERLINGUA

1. Le auto-transfusion in un individo normal de erythrocytos etiquettate per Cr51 o le transfusion de erythrocytos assi etiquettate ab un individo normal a un compatibile recipiente normal es un valide metodo pro mesurar le superviventi transfinzional de ille cellulas. Le metodo es specialmente utile pro determinar le efecto varie factores de collection e de magazinage exerce super le sanguine usate in transfusiones.

2. Le transfusion a in un recipiente normal de erythrocytos etiquettate per Cr51 ab un patiente qui es sub le suspicion que su erythrocytos suffre de un anormalitatem que affice lor superviventi es un satisfactorissime metodo pro verificar le existentia de alterationes del erythrocytos.
3. Quando le auto-transfusion de erythrocytos etiquettate per Cr⁴⁺ es usate pro determinar le superviventia de erythrocytos in patientes qui suffre de phénomenos hemolytic, le valores obtenite debe esser corrigite in considerazione del variationes del volumine erythrocytic que es causate per le tempo del production de nove erythrocytos. Le validitate de tal correctiones per repetite determinariones del circulante massa erythrocytic es limitate per le limites del exactitude del methodo usate. Pro objectivos clinic un methodo satisfactori pare esser be determination del volumimie del massa erythrocytic ab 'omenciamento e al flu periodo de observation con frequente mesurationes hematocritic durante le dies interime.

4. Le indice hemolytic se trova generalmelite satis ben in harmonia comi be resultatos del studios de superviventia de erythroeytos per medio de etiquettage a Cr⁴⁺ si le valores obtenite es corrigite in consideration del variationes del massa erythrocytic.

REFERENCES

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