Nineteen years of experience with autotransfusion for elective surgery in children: more troublesome than we expected

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BACKGROUND: Under the rationale that children undergoing elective surgery are the best candidates for autologous blood donors because of their long life expectancy, aggressive donations of autologous blood, even from infants, have been reported. A number of problems are associated with the procedure, however, whereas the risks of homologous blood are very low.
STUDY DESIGN AND METHODS: From 1987 through 2005, of 5792 patients referred to blood transfusion services at two Japanese university hospitals for autologous blood donations, 314 children younger than 16 years old served as subjects for assessment.
RESULTS: Of 314 children, 7 were not suitable as autologous donors. In most cases this was due to uncooperative behavior. Over a follow-up period of 19 years, the authors encountered 53 cases (17.3%) of donation-related problems, and this rate was higher than the 6 percent rate recorded for adult cases (316/5305). Nine children suffered crucial complications such as vasovagal reactions, and one 14-year-old boy required a vasopressor drug. Important findings were that 6 of these were first-time donors, and the amount of blood drawn was under 10 percent of their estimated blood volume.
CONCLUSION: Of 53 donation-related problems, 9 (17.0%) were accompanied by marked hypotension. Drawing autologous blood from children has become easier with advanced devices; however, lessening of anxiety and tension are essential for the safety of children's autologous blood donation programs. Aggressive donation should be avoided.

The purpose of children's autotransfusion is, as in the case of adult patients, to avoid adverse events caused by allogeneic blood.[1] Especially in children, a long life expectancy is a driving force for the encouragement of this program, and many reports have emphasized its safety and efficacy, even in infants or small children.[2-4] A few reports have been published, however, regarding donor reactions in children's autologous blood donation. Nineteen years have passed since this program was introduced in our hospital. In view of the continuing controversy about the advantage of autotransfusion,[5,6] we attempted to keep accurate records of problems encountered during the course of autologous blood donation, to assess the significance of this method frankly. Also, a special blood bag for the facilitation of collecting blood from children with narrow veins has been introduced.

MATERIALS AND METHODS

During the period of 1987 through 2005, all patients referred to the blood transfusion service at two university hospitals to donate autologous blood were studied. Informed consent was obtained from every patient and/or their guardians. The final decision as to whether the

ABBREVIATIONS: SCD = sterile connection device; UPN(s) = unique patient number(s); VVR(s) = vasovagal reaction.

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patient was suitable as an autologous donor was made by a transfusionist, who considered such factors as general health (cardiopulmonary function in particular), hemoglobin (Hb) level, patient's understanding of the method, and whether there was an infectious disease.

In Japan, an autologous blood donation program is being carried out in accordance with guidelines in *Autotransfusion: A Manual for Drawing Blood and Its Management,* which was produced by a committee consigned to the Ministry of Health and Welfare in 1994. This is mainly applicable to adult patients, however. We use criteria shown in Table 1, which we made for donor children, taking the above guidelines into account as well. As we accumulated more experience with this program, we found that applying it to children was not so difficult, as long as they were cooperative[2] and as long as we did not have to adhere to strict criteria for selection by age or body weight. As a rule, approximately 10 percent of intravascular blood volume was drawn once a week in a bag containing citrate phosphate dextrose adenine anticoagulant, if the Hb level before each donation was 11 g per dL or more.[7] No blood was collected within 3 days of an operation. Autologous blood was stored in a refrigerator at 4°C until the operation. Blood not used within a permissible storage period of 5 weeks was therefore returned to the patient for rejuvenation, followed by another donation to secure a sufficient amount of blood at the time of surgery. This liquid storage method is called the leap-frog.[8] When the blood volume to be drawn was small, the amount of anticoagulant (blood volume, ×0.14 mL) was adjusted with a sterile connection device (SCD), which connects two tubes of different sizes.[8] Usually, each adult patient received 200 mg of oral iron sulfate daily; for children the dose was 4 mg per kg per day. In addition to iron supplementation, recombinant human erythropoietin (rHuEPO) was prescribed for patients with anemia who required more than 800 mL of autologous blood within a shorter donation period.

One of the problems with donation of autologous blood for children is the narrowness of their veins. In the early years after introduction of this program into our hospital, patients with extremely small veins were sometimes excluded as donor patients. Currently, however, by use of an SCD or a blood bag specially designed for children, drawing blood from children with narrow veins has become much easier than it was before. Figure 1 illustrates

TABLE 1. Criteria for autotransfusion for elective surgery in children

1. Indication
   - A. Planned surgery in need of blood transfusion
   - B. Children with rare blood type and/or with unexpected alloantibodies to high-incidence antigens
   - C. Children with two or more kinds of alloantibodies to RBCs
2. Contraindication
   - A. Uncooperative during donation of blood
   - B. Parents have poor understanding of autotransfusion program
   - C. Children with infectious disease
   - D. Children with uncontrolled anemia
   - E. Children with poor general condition and/or with cardiac disease including: 1) aortic stenosis; 2) cardiac risk status of NYHA classification of III and IV; 3) cyanotic congenital heart disease
   - F. Difficulty with venous access
3. Recommended methods
   - A. Informed consent from children and/or their guardians
   - B. Consideration of age (≥6 years) and body weight (≥25 kg)* *Caution should be employed in treating children younger than 6 years old and/or weighing less than 25 kg
   - C. Hb level before donation (≥11 g/dL)
   - D. Amount of blood volume drawn at one time (≤10 mL/kg body weight or ≤12 percent of one blood volume)
   - E. Donation interval (once a week)
   - F. Adjustment of anticoagulant (28/200×blood volume to be drawn)
   - G. Blood donation within 3 days before surgery is not recommended
   - H. Anesthesia is unnecessary, except when blood donation is carried out at the time of cardiac catheter examination.
   - I. Iron supplementation (3-6 mg/kg/day), orally
   - J. Crystalloid infusion following blood donation

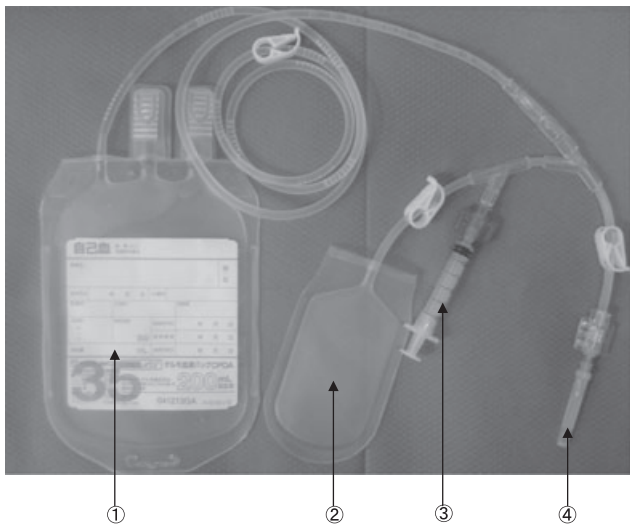

Fig. 1. Special blood bag for children's donation of autologous blood. Anticoagulant in the large bag (1) was moved to the small bag (2), and then approximately 1 mL of it was pulled into a syringe (3). After venipuncture with a needle (4), which had a size corresponding to that of the veins, approximately 9 mL of blood was drawn into a syringe (3) followed by gentle mixing with anticoagulant, and then the mixture was pushed into the large bag (1). This process was repeated carefully until the amount of blood reached the mark a doctor had set.

how to use the special blood bag (TERUFLEX; Terumo, Tokyo, Japan). Recently, when we found it difficult to draw blood at our department due to, for example, restlessness or narrow veins, the blood draw was performed at the time of cardiac catheter examination.[9]

RESULTS

During the investigation period, a total of 5792 patients were referred to our blood transfusion service for donation of autologous blood (Fig. 2). Figure 3 shows the annual change in the number of patients. Until 1996 we saw approximately 200 cases a year, but this number doubled after that, because the first author moved from Fukushima Medical University to Iwate Medical University and promoted the program aggressively. Attention was focused on the number of children under the age of 16 years, because they are not allowed to be volunteer blood donors in Japan; this number increased gradually until 2000, and the recent proportion of children is approximately 3 percent. Over the past 19 years, the total number of children seen was 314 (256 from Fukushima and 58 from Iwate Medical University Hospital). A total of 307 of them actually donated autologous blood, corresponding to 5.5 percent of the entire set of 5612 donor patients.

Figure 4 shows the number of children classified according to the clinical department they were referred to. Of 314 children, 162 were referred to cardiovascular surgery, 98 to orthopedic surgery, and 28 to general pediatrics, and 26 were categorized as miscellaneous. Autologous blood donation was not indicated for 7 children (2.2%, 7/314) and for 173 adults (3.2%, 173/5478) due to various reasons listed in Table 2. Restlessness, excitement, uncooperative behavior, and extremely narrow veins were the main problems related to children's phlebotomy, whereas problems with adult patients were poor general condition, virus-carrier state, and retention of inserted catheter. In Japan, patients who are virus carriers are, as a rule, not candidates for autologous blood donors because of the following four main reasons: 1) the benefits of autologous blood are quite reduced, 2) mishandling of blood of those patients may transfer the infection to someone else, 3) doctors and/or nurses may suffer viral infection by pricks with needles contaminated with infectious organisms, and 4) equipment may be polluted due to torn blood bags. In contrast, the rights of patients undergoing surgery with their own blood should be highly respected. Therefore, in every hospital in Japan, autologous blood donation programs for those patients are carried out very carefully, taking into consideration the above factors.

Table 3 shows the characteristics of 307 children who donated autologous blood. There were wide ranges of age,

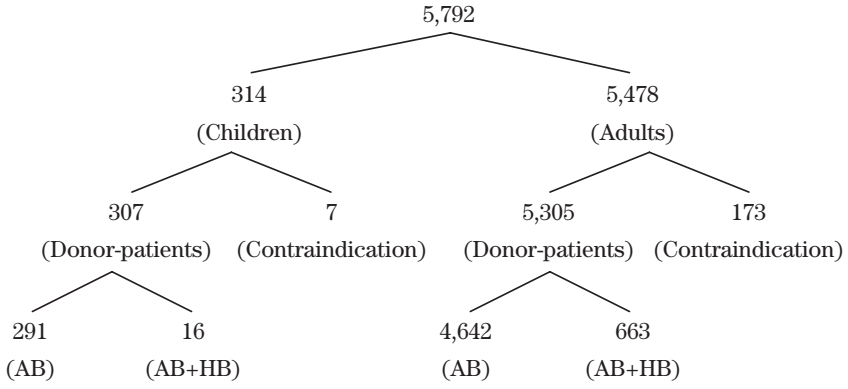

Fig. 2. Distribution of patients. Of 5792 patients, 314 were children under the age of 16 years. Seven cases were excluded as donor patients, and consequently 307 individuals donated autologous blood. A total of 291 of them (94.8%) were operated on without a homologous blood transfusion. AB = autologous blood; HB = homologous blood.

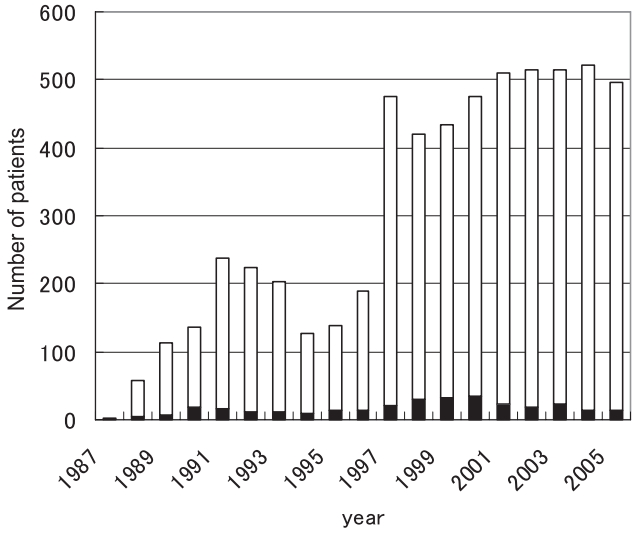

Fig. 3. Time course change of number of patients. (□) Number of adults; (■) children.

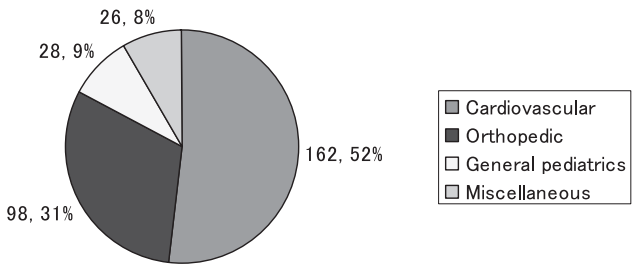

Fig. 4. Number of patients classified by clinical department.

body weight, donation period, and the total amount of blood collected. These were due mainly to the different surgical procedures the patients underwent. Blood was usually used within the permissible storage period of 5 weeks, but rejuvenation was carried out for 28 children (9.1%, 28/307). For 33 infants with cardiovascular disease, donation of autologous blood was carried out during cardiac catheter examination, and this accounts for the reported variation. The mean age (range), body weight, and blood volume donated at one time for those 33 infants were 5 (2-13) years, 18 (11-61) kg, and 154 (100-200) mL, respectively. The proportion of children avoiding homologous blood transfusion was 94.8 percent (291/307), which was apparently higher than that for adult patients (87.5%, 4642/5305).

Over 19 years, the authors encountered a total of 53 children with donation-related problems, and this incidence (17.3%, 53/307) was apparently higher than that for adult patients (6.0%, 316/5305). Table 4 gives more information regarding these problems. Restlessness, postponement of surgery (due mainly to respiratory infection), and narrow veins were the major issues for children. For adult patients, in contrast, donor reactions and poor recovery from phlebotomy-induced anemia in spite of iron supplementation were the most common problems.

Table 5 shows the details of donor reactions involving hypotension observed in nine children. It is not necessarily easy to distinguish vasovagal reactions (VVRs) from hypovolemic hypotension; however, four patients (unique patient numbers [UPNs] 6-9) might have suffered VVR in light of physiologic features such as bradycardia. Three of them (UPNs 6, 8, and 9) felt sick before completion of blood donation. The others experienced nausea or hypotension just after the procedure. This was especially notable for two children (UPNs 4 and 5), for whom hypovolemic hypotension rather than VVR might have been the cause of those symptoms. Their symptoms occurred at the fifth donation; furthermore, the amount of blood drawn at one time was more than 10 percent of the total blood volume in each of these cases. Bradycardia was not observed. Only one 14-year-old boy (UPN 4) developed a remarkably low blood pressure (49/22 mmHg). His symptoms disappeared after speedy treatment with crystalloid infusion from the drawing line with SCD, followed by a vasopressor drug (etilefrine HCl, 2 mg). Confusion or autonomic disturbances such as urinary incontinence were not observed, and none of the patients required hospitalization.

Figure 5 shows the time course of changes in mean Hb level. The level usually falls gradually for 3 weeks after the first donation; this can then be followed by sideways movement. For unknown reasons, however, Hb levels decreased rapidly in two children (13-year-old boy, 27 kg; 13-year-old girl, 46 kg) in spite of sufficient iron supplementation. A fourth donation was postponed and rHuEPO (200 IU/kg) was administered. They resumed blood donations after recovery from anemia and prepared 1000 and 1200 mL of autologous blood, respectively.

TABLE 2. Reasons for exclusion*

Reason	Children	Adults
Excitement, restlessness, etc.	4	
Narrow veins	2	6
Wound infection, decubitus, etc.	1	11
Virus-carrier state		
HBV		27
HCV		49
HTLV-1		1
Retention of inserted catheter		28
Serious anemia		27
Poor general condition		14
Refusal to donate blood		2
Cardiovascular diseases		
Aortic stenosis		2
Poststate of acute myocardial infarction		2
Unstable angina pectoris		2
Arrhythmia		2
Total	7	173

* In addition to poor general condition and/or advanced anemia, patients with aortic stenosis, a poststate of acute myocardial infarction, or unstable angina pectoris were excluded as donor patients. Carriers of viruses such as HBV or HCV were also excluded.

DISCUSSION

The safety of the use of homologous blood has improved remarkably. The risks of transfusion-transmitted viral infection are very low, due to the superb nucleic acid amplification test (NAT). Posttransfusion graft-versus-

TABLE 3. Characteristics of children*

Surgical procedure	Number of patients	Age (years)	Body weight (kg)	Donation period (days)	Amount of blood donated (mL)	Patients avoiding homologous blood transfusion (%)
Cardiovascular	158	7.3 (2-15)	25.9 (11-70)	20 (3-52)	143 (100-1400)	95.6
Orthopedic	95	12.8 (6-15)	42.3 (18-73)	32.9 (3-76)	1079 (200-2200)	90.5
General pediatrics	28	8.6 (1-15)	31.8 (10-60)	18.7 (10-37)	354 (120-1160)	100
Miscellaneous	26	13.2 (11-15)	53.8 (35-77)	13.9 (3-47)	583 (200-1000)	100
Total	307	9.6 (1-15)	33.8 (10-77)	23.3 (3-76)	488.5 (100-2200)	94.8

* Data represent the mean (range).

TABLE 4. Problems related to blood donation

Items	Children	Adults
Discontinuance of blood donation*	19	63
Poor recovery from anemia	7	77
Uncooperative, restlessness, etc.	7	1
Narrow veins	6	19
Sudden fall in blood pressure†	5	12
VVR†	4	7
Indisposition following blood donation‡	4	108
Problems associated with iron sulfate§	1	18
Difficulty in blood transfusion due to macroaggregates		11
Total	53	316

* The autologous blood donation program was discontinued, primarily due to postponement of surgery and aggravation of underlying disease or anemia. Especially in the case of children, respiratory infection was another problem.
† Details are shown in Table 5.
‡ Reasons for indisposition after blood donation included headache, nausea, fatigue, rigors, etc. Thirteen adult patients complained of mild chest discomfort.
§ Problems associated with iron sulfate included eruption, nausea, diarrhea, liver dysfunction, etc.

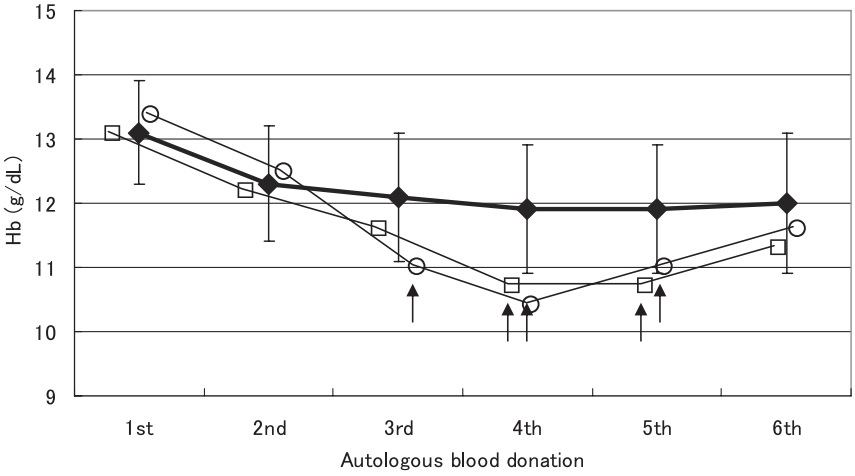

Fig. 5. Change in Hb level during donation period. Bold line indicates the time course change in mean (±SD) Hb level of all the donor children. The two fine lines (○, □) indicate the two children who were given rHuEPO(↑).

host disease is being prevented by radiation. There exists a window period of vulnerability, however, even when the NAT is used.[10] Possible transmission of the SARS virus or of infective prion protein via blood have been reported.[11,12] Transfusion-related acute lung injury has become another issue.[13,14] No conclusion has been reached regarding issues such as immune modulation, for example, the possible suppression of anticancer immune function due to infusion of homologous blood.[15] In light of these issues, autologous blood donation for children's elective surgery is being introduced in many hospitals in Japan. The motivations behind this method are well understood. The real utility of the method, however, as well as its most relevant problems, seem obscure. A major factor in the broad support for this program is the psychological relief felt by children and/or their parents when they undergo an operation with their own blood. The purpose of this report is to reveal problems with children's autologous blood donation that we have encountered during our 19-year experience. We also note the usefulness of SCD and of a special blood bag for donation of autologous blood in children.

The autologous blood donation program is now well established, even for elective surgery in children. The age of eligibility for donor children has decreased. The incidence of avoiding homologous blood during the perioperative period is apparently higher than that for adult patients. Adoption of a longer donation period and a characteristically speedy recovery from phlebotomy-induced anemia enable children to secure a sufficient volume of autologous blood before surgery. These factors may explain the high rate at which they avoid use of homologous blood.[16] The following factors may also influence this observed phenomenon: 1) children have fewer acquired bleeding risks and are less likely to be on antiplatelet therapy, 2) the surgical techniques are different from those for comparable operations in adults, and 3) pediatric surgeons are more likely to use additional blood conservation techniques.

There are few technical problems with the procedure. Even for patients with narrow veins, SCD or the above-mentioned special blood bag enabled us to draw blood easily. These devices for the collection of autologous blood were introduced in our hospital in 1991 and the mean age of 277 children for the years (1991-2005) was 9.5 years, compared with 10.2 for 30 children over 4 years (1987-1990). Because this procedure may involve venipuncture, drawing blood, and crystalloid infusion, however, it sometimes requires a significant amount of time. In cases where children have narrow veins, experience restlessness, or are in need of rejuvenation of old blood due to, for example, postponement of surgery, the procedure often requires more than 1.5 hours. When the blood collection devices were not effective, we were able to obtain the children's own blood at the time of cardiac catheter examination. In our experience with 33 children, who were placed under general anesthesia with close monitoring of cardiopulmonary function, no adverse events occurred.

TABLE 5. Donor reactions of nine children*

Patient	Age, years (male/female)	Disease	Body weight (kg)/one blood volume (mL)	Blood volume drawn at one time (mL)/change in Hb level (g/dL)						Symptoms/treatment
UPN 1	13 (female)	Scoliosis	45/3150	(200)/11.4	200/11.1	200/10.8	0/9.9	200/10.3	200/10.9	Hypotension/crystalloid infusion
UPN 2	15 (male)	VUR	46/4620	(400)/13.7	400/13.4					Hypotension/crystalloid infusion
UPN 3	15 (male)	Coxarthrosis	40/2800	(200)/15.1	200/14.5	200/14.4	200/13.6	200/13.1	200/12.8	Hypotension/crystalloid infusion
UPN 4	14 (male)	Scoliosis	37/2590	300/14.8	300/13.6	200/12.8	300/13.0	(300)/12.6	300/12.4	Shock/crystalloid infusion Vasopressor drug
UPN 5	7 (male)	ASD	22/1540	150/13.0	150/12.6	150/11.5	150/11.8	(200)/12.3	100/11.7	Hypotension/crystalloid infusion
UPN 6	10 (female)	CoA	30/2100	(150)/13.5	200/12.9	150/12.2	150/11.9			VVR/crystalloid infusion
UPN 7	13 (female)	Scoliosis	45/3150	280/12.2	(260)/11.5	200/10.5	260/10.8			VVR/crystalloid infusion
UPN 8	13 (female)	Coxarthrosis	37/2590	(200)/12.1	250/11.7	250/11.0	100/11.3	300/11.3	200/11.5	VVR/crystalloid infusion
UPN 9	7 (male)	VSD	18/1260	(140)/13.5	130/12.3					VVR/crystalloid infusion

* Numbers in parentheses stand for blood volume drawn when the adverse event occurred.
Abbreviations: VUR = vesicoureteral reflux; ASD = atrial septal defect; VSD = ventricular septal defect; CoA = coarctation of the aorta.

This procedure seems to confer a significant benefit to the patient, even from the viewpoint of cost-effectiveness,[17] especially for infants and children who are likely to enjoy longevity. With the use of iron preparations alone, recovery from phlebotomy-induced anemia is faster in these patients than in adult cases. Therefore, there is little need for expensive rHuEPO for donation of autologous blood in children.[18] Of 307 children, only 2 were administered rHuEPO,[19,20] because they became progressively more anemic in spite of normal levels of iron supplementation.

The use of autologous blood is undoubtedly the most ideal transfusion method. We grew uneasy, however, about the high incidence of problems associated with this procedure.[21-23] One of the most serious problems may be VVR, which can involve symptoms such as hypotension, nausea, and pallor that mimic those of hypovolemia, with the exception of bradycardia.[24-26] These symptoms may occur, even if the amount of blood drawn at one time is less than 10 percent of intravascular volume. We encountered nine children who experienced these reactions; six of them were first-time donors. By immediately discontinuing the procedure, elevating the children's legs, and starting crystalloid infusion through the drawing line with the SCD, the symptoms resolved within 15 to 30 minutes. We recognized the importance of relieving their anxiety by engaging them in conversation, letting them watch television, play videos or games, or be attended to by their parents, to improve the safety and success of children's autologous blood donation. We concluded that aggressive donation should be avoided.

In conclusion, the introduction of devices such as SCD or a special blood bag have facilitated autologous blood donation programs for elective surgery in children and have made them easier. The incidence of problems over the past 19 years, however, was higher than we had expected. Of 53 donation-related problems, 9 (17.0%) were accompanied by marked hypotension, despite the fact that the blood volume drawn at one time was less than 10 percent of the estimated blood volume. We recognized that reducing the patients' anxiety and tension, and obtaining good cooperation, are essential for the safety and success of this program for children. We ought to bear in mind that the safety of autologous blood is increasingly sought by the patient and guardian population, even though the safety of homologous blood has improved substantially in recent years.

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