Therapeutic Apheresis and Dialysis

Therapeutic Apheresis and Dialysis 14(1):52–73
doi: 10.1111/j.1744-9987.2009.00716.x

Apheresis Technologies and Clinical Applications: The 2007 International Apheresis Registry

Paul S Malchesky,[1] Anna P Koo,[2] Christine I Skibinski,[2] Angela T Hadsell,[1] and Lisa A Rybicki[2]

[1]The International Center for Artificial Organs and Transplantation, Painesville, and [2]Cleveland Clinic, Cleveland, OH, USA

Abstract: The developments in apheresis technologies and techniques and their clinical applications worldwide are technologically, sociologically, and economically motivated. As in the past apheresis surveys, the statistics have highlighted both the differences by geographic region in clinical practice and in the type of technologies utilized. While a national view of apheresis is very important, an international view may be more representative overall of this therapeutic modality than national results that are highly dependent on the local economics and the available technologies. These regional differences have provided a basis for scientific and clinical assessment of these apheresis technologies and their clinical outcomes, and have impacted the marketing and business developments of new technologies worldwide. The results of the International Apheresis Registry for 2007 report data from 20 centers on five continents. The survey collected data exclusively via a secure internet website on 1735 patients for a total of 6787 treatments. As with our prior registry for 2005, information on stem cell infusions was gathered. Information collected included patients demographics, medical history, treatment diagnoses, treatment specifics (type, methodology, access type, anticoagulants, drugs, and equipment usage), side effects, clinical response, and payment provider. As in prior International Apheresis Registries for 1983, 2000, 2002, and 2005, the survey results highlight the regional differences in apheresis usage and treatment methodologies indicating that an international overview of apheresis may be more representative of the impact of this therapeutic modality. **Key Words:** Registry, Survey, Therapeutic apheresis.

Surveys of apheresis have shown both the differences by geographic region in clinical practices and in the types of technologies utilized (1–5). The first International Apheresis Registry was conducted in 1983 (1) following a pilot survey to demonstrate the feasibility of collecting data and assessing the data collection methodology (6). This first data collected indicated regional differences regarding the apheresis technologies that were applied and the disease states that were treated.

In 2001 the results of the 2000 International Apheresis Registry were reported (3), in 2004 the results of the 2002 International Apheresis Registry (4), and in 2007 the results of the 2005 International Apheresis Registry were reported (5). The present survey's format was essentially the same as the past surveys and was meant to assess the present state of apheresis, the technologies utilized, and the clinical applications. These results were presented in part at the 2009 World Apheresis Association–International Society for Apheresis (WAA–ISFA) Argentina Congress in Buenos Aires, Argentina, March 16–20, 2009.

Received March 2009, revised June 2009.
Address correspondence and reprint requests to Dr Paul S Malchesky, International Center for Artificial Organs and Transplantation, 10 W. Erie Street, Suite 200, Painesville, OH 44077, USA. Email: artiforgs@aol.com
Presented in part at the 2009 WAA-ISFA Argentina Congress in Buenos Aires, Argentina, March 16–20, 2009.

METHODS

The data was collected via an electronic questionnaire as shown in Appendix I, similar to the paper and electronic forms used in the 1983, 2000, 2002, and 2005 Registries, in an effort to provide the respondents with a similar format and to allow comparison of the results with those of prior years. As for the 2005 Registry, information on stem cell infusions was also gathered. The forms request patient information including demographics, medical history, specifics of

the treatment, response to apheresis, and payment provider for the year 2007 only. For many of the questions on the form, drop down menus were used to facilitate answering the question. This data solicitation was approved by the Institutional Review Board (IRB) of the Cleveland Clinic and was compliant with the Health Insurance Portability and Accountability Act (HIPAA).

In soliciting responses, 804 apheresis center personnel were notified by email. Through this notification, the individuals were referred to a secure website (https://clinapps.bio.ri.ccf.org/apheresis/) through which they were provided with instructions on how to enter patient data. Participation was completely voluntary and participants were informed that no compensation would be provided. In order to complete this survey and summarize the results, the deadline for the submission of all data for the reporting year of 2007 was December 15, 2008. From the opening of the website through to its closure, periodic reminders were sent to all the potential participating individuals.

In total, data responses were received from 20 centers (37 persons, see Appendix II) on 1735 patients receiving 6787 treatments, dominated by the reporting from the Asian region, but with no data reported from Japan. Data was received from the reporting regions of Asia, Europe, North America, Australia, and Central/South America, where the regions are classified as in previous surveys. Table 1 outlines the geographic distribution of the survey responders and the number of responding centers, the number of patients submitted by each center, and the number of treatments provided. Within each region, results are listed in the order of the country that submitted the largest number of patients to the country that submitted the smallest number of patients. The ordering of regions from this table is used throughout the remainder of this report for consistency. Categorical variables are summarized as frequency counts, with or without percentages. Continuous variables are summarized as the sample size, mean, standard deviation, and median. All data were analyzed using SAS software (SAS Institute, Cary, NC, USA). If data had been recorded completely and accurately by respondents, all numbers presented in this report would be consistent; however, the numbers of total reported treatments on patients may not appear consistent due to the way people complete the questionnaire. This is a flaw with the type of data collection, not an analysis error.

TABLE 1. *Geographical distribution*

Region/Country	Centers	Patients	Treatments
Asia	8	1197	3555
Turkey	3	498	1718
Korea	2	422	1126
Taiwan	1	94	426
Malaysia	1	167	199
India	1	16	86
Europe	8	283	2119
Austria	1	99	743
Italy	2	30	672
Croatia	1	68	387
Greece	1	21	202
Lithuania	1	23	90
Macedonia	1	1	13
Germany	1	41	12
Australia	2	92	615
Australia	2	92	615
North America	1	142	469
United States of America	1	142	469
Central/South America	1	21	29
Argentina	1	21	29
Total	20	1735	6787

RESULTS

Table 2 outlines data on race and gender for 1723 patients for which both race and gender were noted on the questionnaire. Race is summarized for each region and gender so that the percentages represent the total number of patients within the region/gender of interest. Male subjects, like that in the previous registry (5) outnumbered females (51.0% versus 49.0%) but only slightly. Caucasian was the predominant treated race of the patients treated as in the past, with Asian being the second largest.

Table 3 shows the descriptive statistics for age and months from primary diagnosis to first apheresis treatment summarized as the number of patients, mean, standard deviation, and median. The mean age of patients at the time of their apheresis treatment was 41 years, 4 years lower than the 2005 Registry (5). The Asian and Central/South American regions had the lowest mean ages of 38 years for the patients' first treatment, while the Australian region had the oldest at 54 years. The mean interval from primary diagnosis to the first apheresis treatment was 18.3 months, longer that that from the 2005 Registry (14.0 months), varying from a high of 30.6 months for the North American region to a low of 1.9 months for the Central/South American region. The mean number of months from primary diagnosis to first apheresis treatment was more comparable to the 2005 Registry data versus the longer times reported in 2002 (4) of 34.6 months and the 2000 Registry (3) of 31.6 months.

Table 4 shows the treatment diagnosis for the 1622 patients ordered from the most to least common. The percentages represent the percentage of patients within each region. The most common treatment

TABLE 2. *Race and gender by region for 1723 patients*

Gender/Race	Asia		Europe		Australia		North America		Central/South America		Total	
	N	%*	*N*	%*	*N*	%*	*N*	%*	*N*	%*	*N*	%†
Male											879	51.0
Caucasian	278	47.0	132	99.2	36	63.2	78	88.6	10	100	534	31.0
Asian	275	46.5	–	–	2	3.5	–	–	–	–	277	16.1
Malaysian	38	6.4	–	–	1	1.8	–	–	–	–	39	2.3
Black	–	–	1	0.8	–	–	8	9.1	–	–	9	0.5
Australia/Oceania	–	–	–	–	17	29.8	–	–	–	–	17	1.0
Hispanic	–	–	–	–	–	–	2	2.3	–	–	2	0.1
Native American Indian	–	–	–	–	–	–	–	–	–	–	–	–
Other	–	–	–	–	1	1.8	–	–	–	–	1	0.1
Female											844	49.0
Caucasian	235	39.1	146	99.3	20	57.1	43	84.3	10	100	454	26.3
Asian	237	39.4	1	0.7	1	2.9	–	–	–	–	239	13.9
Malaysian	129	21.5	–	–	–	–	–	–	–	–	129	7.5
Black	–	–	–	–	–	–	5	9.8	–	–	5	0.3
Australia/Oceania	–	–	–	–	14	40.0	–	–	–	–	14	0.8
Hispanic	–	–	–	–	–	–	2	3.9	–	–	2	0.1
Native American Indian	–	–	–	–	–	–	1	2.0	–	–	1	0.1
Other	–	–	–	–	–	–	–	–	–	–	–	–

*Percentage according to region and gender. †Percentage according to 1723 patients.

TABLE 3. *Age and interval from diagnosis to apheresis*

Variable/Region	*N*	Mean	SD	Median
Age (years)				
Asia	1184	38	19	38
Europe	273	45	17	47
Australia	92	54	16	55
North America	142	49	17	51
Central/South America	21	38	21	46
Total	1712	41	19	42
Months from primary diagnosis to first apheresis treatment				
Asia	589	14.7	33.9	1.9
Europe	150	22.5	50.1	0.6
Australia	67	17.1	40.1	0.5
North America	129	30.6	53.7	14.9
Central/South America	2	1.9	2.7	1.9
Total	937	18.3	40.7	3.5

diagnosis categories overall were neoplasms (32.2%), nervous system (22.3%), and blood/blood-forming organs (11.5%) that paralleled the data from the Asian region. Regional differences are noteworthy. For the European region, disorders of endocrine/nutrition/metabolic/immunity, nervous system, and symptoms/signs were the top three treatment diagnoses. In the Australian region symptoms/signs was the most frequently treated category. The same top two categories of neoplasms and nervous system were the top two categories in the 2005 Registry (5).

Table 5 gives the numbers and percentages of patients whose primary diagnosis matches their treatment diagnosis based on the general diagnosis

TABLE 4. *Treatment diagnosis for 1622 patients*

Category	Asia		Europe		Australia		North America		Central/South America		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Neoplasm	396	35.7	18	6.5	20	22.0	88	62.9	–	–	522	32.2
Nervous system	245	22.1	61	22.2	22	24.2	31	22.1	3	42.9	362	22.3
Blood/blood-forming organs	137	12.4	34	12.4	12	13.2	3	2.1	–	–	186	11.5
Endocrine/nutrition/metabolic/immunity	39	3.5	63	22.9	2	2.2	–	–	–	–	104	6.4
Musculoskeletal system	93	8.4	1	0.4	1	1.1	–	–	–	–	95	5.9
Genitourinary system	70	6.3	8	2.9	1	1.1	9	6.4	–	–	88	5.4
Circulatory system	47	4.2	24	8.7	5	5.5	4	2.9	1	14.3	81	5.0
Symptoms/signs	2	0.2	41	14.9	27	29.7	5	3.6	–	–	75	4.6
Injury/poisoning	55	5.0	8	2.9	–	–	–	–	–	–	63	3.9
Digestive system	16	1.4	14	5.1	–	–	–	–	–	–	30	1.8
Infectious/parasitic disease	5	0.5	1	0.4	–	–	–	–	3	42.9	9	0.6
Congenital anomalies	–	–	2	0.7	–	–	–	–	–		2	0.1
Pregnancy and child birth	2	0.2	–	–	–	–	–	–	–		2	0.1
Skin and subcutaneous tissue disease	1	0.1	–	–	1	1.1	–	–	–		2	0.1
Respiratory system	1	0.1	–	–	–	–	–	–	–		1	0.1
Total	1109	100	275	100	91	100	140	100	7	100	1622	100

TABLE 5. *Patients whose primary diagnosis matches the treatment diagnosis*

Region	*N*	# match	% match
Asia	1075	984	91.5
Europe	275	207	75.3
Australia	90	58	64.4
North America	140	138	98.6
Central/South America	7	3	42.9
Total	1587	1390	87.6

category (i.e. not on the specific diagnosis). Overall the percentage matched was 87.6% for 1587 patients reported, which was slightly higher than 86.5% found in the 2005 Registry and 84.5% found in the 2002 Registry. The highest percent matches were 98.6% in the North American region and 91.5% in the Asian region.

Table 6 gives the top 10 treatment diagnoses for the 1545 patients reported. Myasthenia gravis, leukemia, and multiple myeloma were the top three treatment diagnoses. Differences exist among the regions. Myasthenia gravis was also the top-ranked treatment diagnosis in the 2005 (5) and 2002 (4) Registries.

Table 7 gives the top 10 treatment diagnoses by the number of treatments for 6141 treatments reported. The largest numbers of treatments were for myasthenia gravis, followed by hypercholesterolemia and then thrombotic thrombocytopenic purpura (TTP) as was seen also in the 2005 Registry (5). Nearly half of the treatments for myasthenia gravis came from the Asian region and all the treatments for hypercholesterolemia were reported from the European region. As in the previous registries, the differences in ranking between the treatment diagnosis (Table 6) and the treatment diagnosis according to the number of number of treatments (Table 7) suggest that the differences in the treatment requirements by disease categories are related to the treatment requirements for the disease, response to apheresis, patients selection, and payment provider.

Table 8 shows the total number of each type of treatment and the number of patients who received each treatment. Plasma exchange only and plasma treatment only were the most common treatment modalities with over 82% of the reported treatments, and comparable to the 2005 Registry with over 60% of all patients. This is the second Registry where data was collected on stem cell infusion. Over 5.6% of the treatments were for stem cell infusion, an increase over the 2005 Registry, for over 24% of all patients treated. The European region reported the highest number of treatments per patient of 10.4 (the mean of all regions was 4.3), where the highest number of

TABLE 6. *Top 10 treatment diagnoses (according to the number of patients) for 1545 patients*

Rank	Asia	Europe	Australia	North America	Central/South America	Total
1	MG (162)	MG (32)	CRP, MG, blood/blood-forming organs (10 each)	NHL (43)	Behçet's disease (3)	MG (219)
2	Leukemia (132)	Hyperlipidemia (31)		MM (19)	GBS, MG, Refsum's disease, TTP (1 each)	Leukemia (143)
3	MM (99)	Hypercholesterolemia (20)		Hodgkin's disease (16)		MM (131)
4	Blood/blood-forming organs (79)	GBS (17)	MM (9)	MG (14)		NHL (109)
5	SLE (78)	TTP (14)	NHL (7)	CRP, other GU system disease (7 each)		Blood/blood-forming organs (91)
6	NHL, other neoplasms (57 each)	Hyperviscosity syndrome (13)	TTP (4)			SLE (79)
7		HUS (11)	Breast cancer, CML, HD, HUS, hyperviscosity syndrome, MS, other endocrine/nutrition/metabolic/immunity, other neoplasm, other nervous system, paraproteinemia, pemphigus vulgaris, RPGN, SLE, vasculitis/non-cutaneous (1 each)	GBS (6)		GBS (73)
8	GBS (49)	Ulcerative colitis (10)		Breast cancer, MS, other neoplasms (3 each)		Other neoplasms (62)
9	Lupus nephritis (39)	Leukemia (9)				TTP (52)
10	TTP (31)	BMT complications, hemolytic anemia, hypertriglyceridemia, MS (6 each)				Hyperviscosity syndrome (40)

BMT, bone marrow transplant; CML, chronic myeloid leukemia; CRP, chronic relapsing polyneuropathy; GBS, Guillain–Barré syndrome; GU, genitourinary; HD, Hodgkin's disease; HUS, hemolytic uremic syndrome; MG, myasthenia gravis; MM, multiple myeloma; MS, multiple sclerosis; NHL, non-Hodgkin's lymphoma; RPGN, rapidly progressing glomerulonephritis; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenic purpura.

TABLE 7. *Top 10 treatment diagnoses according to number of treatments for 6141 treatments*

Rank	Asia	Europe	Australia	North America	Central/South America	Total
1	MG (605)	Hypercholesterolemia (516)	MG (228)	CRP (88)	GBS (5)	MG (1235)
2	GBS (226)	MG (320)	CRP (86)	MG (79)	Behçet's disease, MG, TTP (3 each)	Hypercholesterolemia (516)
3	TTP (224)	Other circulatory system disease (223)	TTP (65)	Other GU system disease (49)		TTP (425)
4	Blood/blood-forming organs (220)	HUS (180)	RPGN (20)	NHL (43)		GBS (335)
5	Leukemia (191)	TTP (111)	Blood/blood-forming organs (15)	MM (32)	Refsum's disease (1)	HUS (272)
6	Hemolytic anemia (161)	Hyperlipidemia (103)	Hyperviscosity syndrome (12)	GBS (29)		Other circulatory system disease (251)
7	SLE (158)	Hypertriglyceridemia (79)	MM (9)	Myeloma kidney (23)		Blood/blood-forming organs (243)
8	Other neoplasms (117)	GBS (75)	NHL, vasculitis/non-cutaneous (7 each)	TTP (22)		CRP (239)
9	MM (115)	Hemolytic anemia, other endocrine/nutrition/metabolic/immunity (62 each)		Other circulatory system disease (20)		Hemolytic anemia (223)
10	Kidney transplant complications (107)		HUS, other endocrine/nutrition/metabolic/immunity, other nervous system diseases, SLE (5 each)	HD (16)		Leukemia (202)

CRP, chronic relapsing polyneuropathy; GBS, Guillain–Barré syndrome; GU, genitourinary; HD, Hodgkin's disease; HUS, hemolytic uremic syndrome; MG, myasthenia gravis; MM, multiple myeloma; NHL, non-Hodgkin's lymphoma; RPGN, rapidly progressing glomerulonephritis; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenic purpura.

TABLE 8. *Treatments and the number of patients receiving the treatment*

Treatment	Asia	Europe	Australia	North America	Central/South America	Total
Plasma exchange only	2217 (516)	1219 (146)	576 (50)	383 (53)	12 (4)	4407 (769)
Plasma treatment only	703 (148)	517 (22)	0 (0)	0 (0)	0 (0)	1220 (170)
Whole blood adsorption only	0 (0)	254 (10)	0 (0)	0 (0)	0 (0)	254 (10)
LDL hemoperfusion	0 (0)	250 (9)	0 (0)	0 (0)	0 (0)	250 (9)
Other type (ADA column)	0 (0)	4 (1)	0 (0)	0 (0)	0 (0)	4 (1)
Cytapheresis only	10 (4)	12 (7)	3 (2)	0 (0)	0 (0)	25 (13)
Lymphoplasmapheresis only	70 (42)	0 (0)	0 (0)	0 (0)	0 (0)	70 (42)
Stem cell infusion only	331 (331)	16 (16)	31 (31)	86 (86)	17 (17)	481 (481)
Autologous	249 (249)	4 (4)	30 (30)	85 (85)	13 (13)	381 (381)
Preparation: chemotherapy	210 (210)	0 (0)	27 (27)	68 (68)	0 (0)	305 (305)
Preparation: chemotherapy and RT	13 (13)	4 (4)	0 (0)	0 (0)	0 (0)	17 (17)
Preparation: G-CSF	0 (0)	0 (0)	0 (0)	17 (17)	13 (13)	30 (30)
Preparation: unspecified	26 (26)	0 (0)	3 (3)	0 (0)	0 (0)	29 (29)
Allogenic	82 (82)	12 (12)	1 (1)	1 (1)	4 (4)	100 (100)
Preparation: chemotherapy	9 (9)	0 (0)	0 (0)	1 (1)	0 (0)	10 (10)
Preparation: chemotherapy and RT	1 (1)	10 (10)	0 (0)	0 (0)	0 (0)	11 (11)
Preparation: G-CSF	1 (1)	0 (0)	0 (0)	0 (0)	4 (4)	5 (5)
Preparation: unspecified	71 (71)	2 (2)	1 (1)	0 (0)	0 (0)	74 (74)
Plasma exchange and plasma treatment	0 (0)	101 (3)	0 (0)	0 (0)	0 (0)	101 (3)
Plasma exchange and autologous stem cells	181 (71)	0 (0)	5 (1)	0 (0)	0 (0)	186 (72)
Plasma treatment and whole blood adsorption	24 (1)	0 (0)	0 (0)	0 (0)	0 (0)	24 (1)
Plasma treatment and cytapheresis	19 (1)	0 (0)	0 (0)	0 (0)	0 (0)	19 (1)
All treatments	3555 (1114)	2119 (204)	615 (84)	469 (139)	29 (21)	6787 (1562)

Number of treatments (number of patients treated). G-CSF, granulocyte colony-stimulating factor; LDL, low-density lipoprotein; RT, radiotherapy.

treatments were for hypercholesterolemia and myasthenia gravis, each disease notably requiring multiple treatments. No plasma treatment or whole blood adsorption procedures were reported in the Australian, North American, and Central/South American regions, likely a reflection of the general limited availability and lack of marketing of such devices in these regions. Technology availability in the different regions influences the type of treatment provided to the patients as well as the disease states treated.

Table 9 shows the number (also shown in Table 8) and percentage of patients who received each type of treatment. Plasma exchange only and plasma treatment accounted for 60.1% of the types of treatments for the 1562 patients reported. Stem cell infusion was used in 30.8% of the patients, up from the 25.7% reported in the 2005 Registry (5). Only 3.5% of the patients were treated by cytapheresis only and lymphoplasmapheresis only.

Table 10 shows the frequencies and percentages of the number of treatments noted for each patient. Most patients received 1–5 treatments, with the exception of whole blood adsorption where most patients receiving this form of treatment received more than 10 treatments. Nearly all patients receiving whole blood adsorption were from the European region where this technology is well known and marketed. This technology is also well represented in

TABLE 9. *Number and percentage of patients receiving each type of treatment*

Treatment	Asia	Europe	Australia	North America	Central/South America	Total
Plasma exchange only	516 (46.3%)	146 (71.6%)	50 (59.5%)	53 (38.1%)	4 (19.0%)	769 (49.2%)
Plasma treatment only	148 (13.3%)	22 (10.8%)	0 (0%)	0 (0%)	0 (0%)	170 (10.9%)
Whole blood adsorption only	0 (0%)	10 (4.9%)	0 (0%)	0 (0%)	0 (0%)	10 (0.6%)
Cytapheresis only	4 (0.4%)	7 (3.4%)	2 (2.4%)	0 (0%)	0 (0%)	13 (0.8%)
Lymphoplasmapheresis only	42 (3.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	42 (2.7%)
Stem cell infusion only	331 (29.7%)	16 (7.8%)	31 (36.9%)	86 (61.9%)	17 (81.0%)	481 (30.8%)
Plasma exchange and plasma treatment	0 (0%)	3 (1.5%)	0 (0%)	0 (0%)	0 (0%)	3 (0.2%)
Plasma exchange and stem cells	71 (6.4%)	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	72 (4.6%)
Plasma treatment and whole blood adsorption	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Plasma treatment and cytapheresis	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.1%)
Number of patients	1114	204	84	139	21	1562

TABLE 10. *Number of treatments given per patient*

Treatment/No. of treatments	Asia		Europe		Australia		North America		Central/South America		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Plasma exchange												
1–5	475	80.9	87	58.4	21	41.2	24	45.3	4	100.0	611	72.4
6–10	89	15.2	32	21.5	9	17.6	18	34.0	0		148	17.5
>10	23	3.9	30	20.1	21	41.2	11	20.7	0		85	10.1
(No. of pts)	(587)		(149)		(51)		(53)		(4)		(844)	
Plasma treatment												
1–5	131	87.3	4	16.0	0	–	0	–	0	–	135	77.1
6–10	14	9.3	3	12.0	0	–	0	–	0	–	17	9.7
>10	5	3.3	18	72.0	0	–	0	–	0	–	23	13.1
(No. of pts)	(150)		(25)		(0)		(0)		(0)		(175)	
Whole blood adsorption												
1–5	0	0	3	30.0	0	–	0	–	0	–	3	27.3
6–10	0	0	0	0.0	0	–	0	–	0	–	0	0.0
>10	1	100	7	70.0	0	–	0	–	0	–	8	72.7
(No. of pts)	(1)		(10)		(0)		(0)		(0)		(11)	
Cytapheresis												
1–5	5	100	7	100	2	100	0	–	0	–	14	100
6–10	0	0	0	0	0	0	0	–	0	–	0	0
>10	0	0	0	0	0	0	0	–	0	–	0	0
(No. of pts)	(5)		(7)		(2)		(0)		(0)		(14)	
Lymphoplasmapheresis												
1–5	42	100	0	–	0	–	0	–	0	–	42	100
6–10	0	0	0	0	0	0	0	–	0	–	0	0
>10	0	0	0	–	0	–	0	–	0	–	0	0
(No. of pts)	(42)		(0)		(0)		(0)		(0)		(42)	
Stem cell infusion												
1–5	402	100	16	100	32	100	86	100	17	100	553	100
6–10	0	0	0	0	0	0	0	–	0	–	0	0
>10	0	0	0	0	0	0	0	–	0	–	0	0
(No. of pts)	(402)		(16)		(32)		(86)		(17)		(553)	

Japan, but there was no reporting from Japan in this registry year.

Table 11 gives the average volume of plasma exchange, plasma treatment and whole blood adsorption, and the average number of cells for cytapheresis, lymphoplasmapheresis and stem cell infusions. The mean volume exchanged for plasma exchange was 3.1 L, for plasma treatment 2.7 L, and for whole blood adsorption 7.8 L. The lower volume treated for plasma treatment versus plasma exchange is unexplained yet interesting, considering that with plasma treatment higher volumes should be treatable as generally plasma replacement products are not required and plasma constituent dilution is of lesser concern. The high mean whole blood adsorption relates to the high average volume treatment in the European region. These were no reported data for lymphoplasmapheresis in this registry. The average number of cells removed in cytapheresis was 44.9×10^{11} cells and the average number of stem cells infused was 13.9×10^{6}/kg, which was comparable to that reported in the 2000 Registry and lower than that reported in the 2002 Registry. In particular, higher volumes of stem cells were infused in the Asian and European regions.

Table 12 gives the number of treatments per replacement solution types and the number of patients treated with each. Patients may have received more than one type of solution, therefore the categories are not mutually exclusive. Albumin solution, as in past registries, was the most common replacement solution, followed by fresh frozen plasma, and then electrolyte solution as in previous surveys.

Table 13 summarizes the equipment types reported and Table 14 the plasma membrane separators. Table 15 gives the plasma treatment methods of membrane filtration (cascade filtration), sorption, or other methods; Table 16 gives the plasma membrane treatment devices used; and Table 17 gives the sorptive plasma treatment devices reportedly used. For the equipment type the most frequently reportedly used were those of Gambro, Fresenius, Kuraray and B Braun. For the membrane plasma separation devices the order of reported use was Asahi, Kuraray, Gambro, and Hospal. For the plasma membrane (cascade) treatment the order of reported device use was Asahi, Kuraray, Fresenius, and B Braun; and for plasma sorption treatment Kaneka and then Fresenius. As in past surveys, plasma treatments by membrane (cascade) plasma treatment and sorption were

TABLE 11. *Treatment volumes and cells*

Variable/Region	*N*	Mean	SD	Median
Plasma exchange, average volume (L)				
Asia	513	3.0	0.8	3.0
Europe	146	3.1	0.9	3.0
Australia	51	4.7	9.4	3.0
North America	49	2.9	0.6	3.0
Central/South America	4	1.9	0.1	1.9
Total	763	3.1	2.6	3.0
Plasma treatment, average volume (L)				
Asia	147	2.6	0.5	2.7
Europe	23	3.5	1.1	3.0
Australia	0	–	–	–
North America	0	–	–	–
Central/South America	0	–	–	–
Total	170	2.7	0.7	2.8
Whole blood adsorption, average volume (L)				
Asia	1	2.6	–	2.6
Europe	9	8.3	4.0	9.9
Australia	0	–	–	–
North America	0	–	–	–
Central/South America	0	–	–	–
Total	10	7.8	4.2	9.3
Cytapheresis, average number of cells ($\times 10^{11}$)				
Asia	4	2.2	0.6	2.1
Europe	6	8.4	4.0	7.5
Australia	2	240.0	113.1	240.0
North America	0	–	–	–
Central/South America	0	–	–	–
Total	12	44.9	97.4	6.0
Lymphoplasmapheresis, average number of cells ($\times 10^{10}$)				
Asia	0	–	–	–
Europe	0	–	–	–
Australia	0	–	–	–
North America	0	–	–	–
Central/South America	0	–	–	–
Total	0	–	–	–
Lymphoplasmapheresis, average volume (L)				
Asia	0	–	–	–
Europe	0	–	–	–
Australia	0	–	–	–
North America	0	–	–	–
Central/South America	0	–	–	–
Total	0	–	–	–
Stem cell infusion, average number of cells ($\times 10^{6}$/kg)				
Asia	367	16.2	35.5	7.0
Europe	17	12.2	19.4	7.0
Australia	31	7.6	9.5	5.0
North America	85	8.9	14.8	4.0
Central/South America	17	4.1	1.6	4.0
Total	517	13.9	31.0	6.0

only reported from the Asian and European regions, likely reflecting the general unavailability or lower use of those treatment methods in the other regions.

Table 18 gives the number of treatments per blood access method and the number of patients who received each method. As in prior surveys, venous access methods are by far the most frequently used blood access methods, with the most frequently used methods as peripheral veno-venous, central venous, and access via the femoral vein. As in past surveys, the use of arterial puncture in the Asian region and the use of an arteriovenous fistula/shunt is likely related to the procedures under the direction of dialysis centers versus blood banks.

Table 19 gives the anticoagulant and drug usages. The primary anticoagulants used are citrate and heparin. For all patients treated, 65% were reported as taking no steroids or immunosuppressives, with 20.6% of the patients receiving steroids only. As in past surveys, the differences in drug regimes in the different regions and among the patients are related to patient diagnoses.

Table 20 gives the number of side effects or complications during the treatment and up to 2 h after its cessation. Blood access difficulties, which have ranked high in past surveys, was the most noted complication. One death was reported in this survey.

Table 21 gives the reported responses to apheresis and payment provider. Improvement was noted in 59.5% of the patients with 16.5% reporting the condition as same. A relatively high response of 20.0% was noted as not assessable. Response to apheresis was determined objectively, at least in part, in 87.6% of cases. Regarding the payment provider, 60.8% of patient treatments were provided at least in part by the government, down from over 70% from the 2005 and 2002 surveys. In the North and Central/South American regions very significantly 69.0% and 95.2%, respectively, received support from private insurance. As in past surveys, the Asian region reported the highest self/family payment in this survey of 10.8% and the European region reported the highest hospital/institution payment of 45.2%

DISCUSSION

In the report of the 2005 International Apheresis Registry (5) a discussion of the various reported national apheresis registries was given, as well as for the World Apheresis Registry (7). While there have been reported only minor changes to the discussion (the Korean Registry report was published) we include here a brief overview of these reports. Tables 22–24 summarize the overall results from these surveys. National apheresis registry reports have been published from Canada (8), France (9), Germany (10), Hungary (11), Italy(12,13), Japan (14,15), most recently Korea (16), Philippines (17), the United States of America (USA) (2,18), and Venezuela (19).

From a review of the national registry reports, it is noteworthy that procedures are not formally registered with few exceptions, data collection is not uniform or centralized with few exceptions, and the numbers of procedures are believed to be underreported. Also, the cases/diagnoses treated vary

TABLE 12. *Replacement solution*

Solution	Asia	Europe	Australia	North America	Central/South America	Total
Albumin solution	1393 (430)	535 (105)	512 (47)	192 (24)	9 (3)	2641 (609)
Fresh frozen plasma	1117 (283)	654 (56)	112 (10)	28 (3)	3 (1)	1914 (353)
Electrolyte solution	578 (207)	13 (9)	0 (0)	0 (0)	0 (0)	591 (216)
Plasma expander solution	209 (46)	0 (0)	0 (0)	0 (0)	0 (0)	209 (46)
Purified protein fraction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Plasma products	2 (1)	0 (0)	0 (0)	4 (1)	0 (0)	6 (2)
Other	154 (29)	21 (10)	11 (2)	169 (26)	0 (0)	355 (67)
Albumin + hespan + NSS	0 (0)	0 (0)	0 (0)	169 (26)	0 (0)	169 (26)
Cryosupernatant	98 (8)	0 (0)	0 (0)	0 (0)	0 (0)	98 (8)
Albumin + fresh frozen plasma	56 (21)	0 (0)	0 (0)	0 (0)	0 (0)	56 (21)
Red blood cells	0 (0)	7 (6)	11 (2)	0 (0)	0 (0)	18 (8)
Albumin + saline	0 (0)	9 (2)	0 (0)	0 (0)	0 (0)	9 (2)
HAES	0 (0)	4 (1)	0 (0)	0 (0)	0 (0)	4 (1)
Autologous plasma	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)

Number of treatments (number of patients treated). HAES, hydroxyethyl starch; NSS, normal saline solution.

country by country and are influenced by the recognized medical evidence for treatment of specific conditions/diseases, the individual clinician's expertise and training in the apheresis techniques, the facilities offered for treatment such as blood centers or dialysis centers, for example, the reimbursement policies and treatment costs, and available technologies. The availability of technologies impacts the procedural methodologies used, including the types of equipment, anticoagulation, blood access methods, and even the diseases treated.

The format of the questionnaire used for their survey was very similar to that used for the prior surveys (1,3–5). As in the previous surveys (4,5), this survey was conducted through a secure dedicated website.

TABLE 13. *Equipment type*

Equipment	Asia	Europe	Australia	North America	Central/South America	Total
Asahi Plasauto	264 (55)	0 (0)	0 (0)	0 (0)	0 (0)	264 (55)
Gambro BCT COBE Spectra, Spectra LRS	1804 (491)	500 (63)	667 (86)	714 (134)	0 (0)	3685 (774)
Baxter (Fenwal) CS 3000/3000 Plus	11 (4)	0 (0)	0 (0)	0 (0)	0 (0)	11 (4)
Fresenius A 2008 PF	3 (1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)
Gambro BCT COBE AK100/AK100 Ultra	0 (0)	0 (0)	0 (0)	14 (3)	0 (0)	14 (3)
Kuraray	426 (94)	0 (0)	0 (0)	0 (0)	0 (0)	426 (94)
Self-Assembled	14 (3)	0 (0)	0 (0)	0 (0)	0 (0)	14 (3)
Baxter (Fenwal) Accura	3 (1)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)
Baxter (Fenwal) Amicus	153 (126)	0 (0)	0 (0)	0 (0)	0 (0)	153 (126)
Baxter (Fenwal) Autopheresis C	0 (0)	82 (20)	0 (0)	0 (0)	0 (0)	82 (20)
B Braun Diapact	201 (100)	162 (37)	0 (0)	0 (0)	0 (0)	363 (137)
B Braun Plasmat Secura	0 (0)	23 (1)	0 (0)	0 (0)	0 (0)	23 (1)
Excorim (Fresenius)	0 (0)	160 (7)	0 (0)	0 (0)	0 (0)	160 (7)
Fresenius 4008 ADS	23 (1)	165 (5)	0 (0)	0 (0)	0 (0)	188 (6)
Fresenius AS 104, 204	844 (216)	54 (15)	0 (0)	0 (0)	6 (4)	904 (235)
Fresenius Comtec	331 (118)	34 (15)	0 (0)	0 (0)	50 (19)	415 (152)
Haemonetics PCS2 System	0 (0)	6 (4)	0 (0)	0 (0)	0 (0)	6 (4)
Hospal Prisma	0 (0)	143 (35)	0 (0)	0 (0)	0 (0)	143 (35)
Kaneka	0 (0)	248 (9)	0 (0)	0 (0)	0 (0)	248 (9)
Otsuka Adamonitor MN6-N	0 (0)	24 (3)	0 (0)	0 (0)	0 (0)	24 (3)
Therakos UVAR XTS	0 (0)	204 (15)	0 (0)	0 (0)	0 (0)	204 (15)
Other	9 (1)	268 (16)	0 (0)	0 (0)	0 (0)	277 (17)
B Braun Plasmat Futura	0 (0)	133 (5)	0 (0)	0 (0)	0 (0)	133 (5)
Fresenius Dali	0 (0)	85 (4)	0 (0)	0 (0)	0 (0)	85 (4)
Lipocollect 200-Adasorb	0 (0)	21 (1)	0 (0)	0 (0)	0 (0)	21 (1)
Gambro AK-10	0 (0)	13 (1)	0 (0)	0 (0)	0 (0)	13 (1)
Diamed Octo Nova	0 (0)	10 (2)	0 (0)	0 (0)	0 (0)	10 (2)
Kuraray 8300	9 (1)	0 (0)	0 (0)	0 (0)	0 (0)	9 (1)
Fresenius Multifiltrate	0 (0)	6 (3)	0 (0)	0 (0)	0 (0)	6 (3)

Number of treatments (number of patients treated).

TABLE 14. *Plasma membrane separator types*

Type	Asia	Europe	Australia	North America	Central/South America	Total
Asahi	630 (224)	602 (32)	0 (0)	0 (0)	0 (0)	1232 (256)
Cobe	13 (4)	0 (0)	0 (0)	0 (0)	0 (0)	13 (4)
Fresenius	9 (2)	104 (5)	0 (0)	0 (0)	0 (0)	113 (7)
Gambro	0 (0)	196 (40)	0 (0)	0 (0)	0 (0)	196 (40)
Kuraray	432 (95)	0 (0)	0 (0)	0 (0)	0 (0)	432 (95)
Other	0 (0)	339 (46)	0 (0)	0 (0)	0 (0)	339 (46)
Hospal Prisma TPE Set	0 (0)	178 (38)	0 (0)	0 (0)	0 (0)	178 (38)
B Braun	0 (0)	79 (5)	0 (0)	0 (0)	0 (0)	79 (5)
Citem 10	0 (0)	11 (1)	0 (0)	0 (0)	0 (0)	11 (1)
Not specified	0 (0)	71 (2)	0 (0)	0 (0)	0 (0)	71 (2)

Number of treatments (number of patients treated).

TABLE 15. *Plasma treatment methods*

Method	Asia	Europe	Australia	North America	Central/South America	Total
Cascade	666 (135)	192 (13)	0 (0)	0 (0)	0 (0)	858 (148)
Sorption	16 (1)	607 (26)	0 (0)	0 (0)	0 (0)	623 (27)
Other	9 (1)	293 (14)	0 (0)	0 (0)	0 (0)	302 (15)
B Braun Plasmat Futura	0 (0)	133 (5)	0 (0)	0 (0)	0 (0)	133 (5)
Precipitation	0 (0)	79 (5)	0 (0)	0 (0)	0 (0)	79 (5)
LDL Precipitation (HELP)	0 (0)	35 (1)	0 (0)	0 (0)	0 (0)	35 (1)
PCPP	9 (1)	0 (0)	0 (0)	0 (0)	0 (0)	9 (1)
4A Filter	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Not specified	0 (0)	45 (2)	0 (0)	0 (0)	0 (0)	45 (2)

Number of treatments (number of patients treated).

TABLE 16. *Plasma membrane treatment devices*

Product	Asia	Europe	Australia	North America	Central/South America	Total
Asahi	445 (184)	440 (25)	0 (0)	0 (0)	0 (0)	885 (209)
Fresenius	4 (1)	104 (5)	0 (0)	0 (0)	0 (0)	108 (6)
Kuraray	536 (116)	0 (0)	0 (0)	0 (0)	0 (0)	536 (116)
Other	0 (0)	80 (6)	0 (0)	0 (0)	0 (0)	80 (6)
B Braun	0 (0)	79 (5)	0 (0)	0 (0)	0 (0)	79 (5)
Evaflux	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)

Number of treatments (number of patients treated).

TABLE 17. *Sorptive plasma treatment devices*

Method	Asia	Europe	Australia	North America	Central/South America	Total
Asahi	4 (2)	66 (2)	0 (0)	0 (0)	0 (0)	70 (4)
Kaneka	0 (0)	207 (8)	0 (0)	0 (0)	0 (0)	207 (8)
Other	16 (1)	414 (15)	0 (0)	0 (0)	0 (0)	430 (16)
Fresenius Dali	0 (0)	85 (4)	0 (0)	0 (0)	0 (0)	85 (4)
LDL-Therasorb-Columns	0 (0)	71 (2)	0 (0)	0 (0)	0 (0)	71 (2)
Excorim, Fresenius	0 (0)	62 (1)	0 (0)	0 (0)	0 (0)	62 (1)
Lipocollect 200-Adasorb	0 (0)	56 (2)	0 (0)	0 (0)	0 (0)	56 (2)
Fresenius ADS 4800	0 (0)	42 (1)	0 (0)	0 (0)	0 (0)	42 (1)
Citem 10	0 (0)	27 (3)	0 (0)	0 (0)	0 (0)	27 (3)
B Braun Plasmat Futura	0 (0)	22 (1)	0 (0)	0 (0)	0 (0)	22 (1)
Lipopak	16 (1)	0 (0)	0 (0)	0 (0)	0 (0)	16 (1)
Not specified	0 (0)	49 (1)	0 (0)	0 (0)	0 (0)	49 (1)

Number of treatments (number of patients treated).

TABLE 18. *Blood access methods*

Method	Asia	Europe	Australia	North America	Central/South America	Total
Peripheral veno-venous	630 (263)	2373 (178)	397 (57)	37 (8)	1 (1)	3438 (507)
Central venous	2601 (584)	475 (70)	111 (21)	675 (130)	55 (20)	3917 (825)
Femoral vein	978 (316)	18 (5)	55 (4)	1 (1)	0 (0)	1052 (326)
Arteriovenous fistula/shunt	48 (25)	212 (13)	16 (3)	29 (4)	0 (0)	305 (45)
Arterial puncture	21 (6)	0 (0)	0 (0)	0 (0)	0 (0)	21 (6)
Other	28 (6)	15 (1)	81 (5)	2 (1)	0 (0)	126 (13)
Port-a-cath	0 (0)	0 (0)	76 (4)	0 (0)	0 (0)	76 (4)
Hickman	23 (5)	0 (0)	0 (0)	0 (0)	0 (0)	23 (5)
Permcath	0 (0)	15 (1)	0 (0)	0 (0)	0 (0)	15 (1)
B Braun Plasmat	5 (1)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1)
Via ECMO	0 (0)	0 (0)	0 (0)	2 (1)	0 (0)	2 (1)
Not specified	0 (0)	0 (0)	5 (1)	0 (0)	0 (0)	5 (1)

Number of treatments (number of patients treated).

Of the 804 persons solicited, data was received from 39 individuals representing a 4.9% response rate, which is the highest response rate in recent surveys. Reporting was from 20 centers on five continents. All reporting is voluntary and there is no financial support provided to the reporting centers or individuals. We are deeply indebted to all the centers and collaborative persons that supported this Registry. (See Appendix II for listings of the participating hospitals and clinics and collaborative persons.) Considering the voluntary nature of this survey, we were pleased at this response rate.

In reviewing the survey results one must be considerate of the response rate and the sources of the responses. The geographic distribution of the individual survey responders can have a very important influence of the results reported. Based on the populations in the various regions reporting, the centers reporting are not necessarily representative of the therapeutic apheresis activities in their regions.

This survey included reports of 1735 patients, the most ever reported in this survey design, and 53% higher than that of the next highest patient numbers reported in 2005 (5) from 20 centers on five continents. The Asian region reported by far the majority of the patients (69%), despite no reporting from Japan. The number of treatments reported was 6787, which are in line with that reported in 2005. As in prior registries, the highest treatment populations were Caucasians, followed by Asians, with a more equal distribution of male and female (51.0% versus 49.0%). The mean age of treatment reported of 41 years was four years less than in the past registries. The top treatment diagnostic category was neoplasms, displacing the traditional front runner of nervous system disorders in previous surveys. The top treatment diseases were myasthenia gravis, leukemia, multiple myeloma, non-Hodgkin's lymphoma, and other diseases of blood/blood-forming organs. Regional differences are noteworthy, for example in the European region the treatments of hyperlipi-

TABLE 19. *Anticoagulants and drugs*

	Asia		Europe		Australia		North America		Central/South America		Total	
Type	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Anticoagulants												
Citrate only	596	49.8	83	29.3	90	97.8	55	40.4	4	19.0	828	47.9
Heparin only	188	15.7	105	37.1	0	0.0	0	0.0	0	0.0	293	16.9
Heparin and citrate	301	25.1	72	25.4	2	2.2	81	59.6	17	81.0	473	27.4
None	112	9.4	20	7.1	0	0.0	0	0.0	0	0.0	132	7.6
Other (saline flush)	0	0.0	3	1.1	0	0.0	0	0.0	0	0.0	3	0.2
No. of patients	1197		283		92		136		21		1729	
Drugs												
None	780	65.2	173	61.1	56	60.9	97	68.3	21	100.0	1127	65.0
Steroids only	241	20.1	81	28.6	24	26.1	11	7.7	0	0.0	357	20.6
Steroids and immunosuppressive	157	13.1	24	8.5	12	13.0	30	21.1	0	0.0	223	12.9
Immunosuppressive only	19	1.6	5	1.8	0	0.0	4	2.8	0	0.0	28	1.6
No. of patients	1197		283		92		142		21		1735	

%, percentage of patients; N, number of patients.

TABLE 20. *Side effects or complications during or up to 2 hours following treatment*

Side effect/complication	Asia	Europe	Australia	North America	Central/South America	Total
Hypotension	59 (41)	40 (26)	19 (10)	7 (6)	1 (1)	126 (84)
Blood access difficulties	136 (89)	155 (50)	59 (18)	2 (1)	0 (0)	352 (158)
Bleeding: access site	6 (6)	1 (1)	0 (0)	1 (1)	0 (0)	8 (8)
Bleeding: other site	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	1 (1)
Shock	6 (6)	0 (0)	0 (0)	0 (0)	0 (0)	6 (6)
Fever/chills	53 (34)	8 (5)	19 (2)	0 (0)	0 (0)	80 (41)
Circuit clotting	1 (1)	21 (18)	0 (0)	0 (0)	0 (0)	22 (19)
Allergic reaction	65 (32)	43 (21)	26 (1)	0 (0)	0 (0)	134 (54)
Hemolysis	55 (36)	0 (0)	0 (0)	0 (0)	0 (0)	55 (36)
Pain other than at access site	3 (3)	1 (1)	1 (1)	0 (0)	0 (0)	5 (5)
Respiratory distress	6 (6)	3 (3)	2 (2)	0 (0)	0 (0)	11 (11)
Death	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
ACE-inhibitor related effects	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Arrhythmia/tachycardia/myocardial infarction	4 (4)	3 (3)	5 (5)	0 (0)	0 (0)	12 (12)
Citrate-induced reaction	1 (1)	68 (22)	69 (19)	0 (0)	0 (0)	138 (42)
Device-related malfunction	26 (18)	16 (13)	0 (0)	0 (0)	0 (0)	42 (31)
Headache	7 (7)	8 (7)	0 (0)	0 (0)	0 (0)	15 (14)
Hypocalcemia	55 (41)	3 (1)	52 (13)	0 (0)	0 (0)	110 (55)
Hypertension	6 (6)	10 (5)	0 (0)	0 (0)	0 (0)	16 (11)
Nausea	13 (11)	18 (12)	8 (5)	0 (0)	0 (0)	39 (28)
Paresthesia	56 (32)	8 (3)	84 (22)	2 (1)	0 (0)	150 (58)
Others	39 (32)	3 (3)	17 (2)	2 (1)	0 (0)	61 (38)
Abdominal pain	4 (4)	0 (0)	0 (0)	0 (0)	0 (0)	4 (4)
Anxiety	5 (5)	0 (0)	0 (0)	0 (0)	0 (0)	5 (5)
Bone pain	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Chest discomfort	5 (3)	0 (0)	0 (0)	0 (0)	0 (0)	5 (3)
Chest pain, S_PO_2 decrease	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Chest stuffiness	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Cold	0 (0)	0 (0)	16 (1)	0 (0)	0 (0)	16 (1)
Confusion	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Cramping	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Deep vein thrombosis	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Diarrhea, Abdomen pain	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Disposable	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Electricity failure	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Epistaxis	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Fever	1 (1)	1 (1)	0 (0)	0 (0)	0 (0)	2 (2)
Flush	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Itching	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)
Itching, skin rash	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
KD TPL site pain	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Nasal bleeding	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Pain in knees	0 (0)	0 (0)	0 (0)	2 (1)	0 (0)	2 (1)
Pain of jugular catheter site	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Palpitation	2 (2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2)
Palpitation, dizziness	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
Panic	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	1 (1)
Toe pain control use morphine	5 (1)	0 (0)	0 (0)	0 (0)	0 (0)	5 (1)
User mistake	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)

Number of episodes (number of patients). ACE, angiotensin converting enzyme.

demia and hypercholesterolemia were more commonplace, but regional differences exist, also dependent on reimbursement, the physician's knowledge, and the technical expertise and technologies available (equipment types).

Depending on the treatment diagnosis, the number of treatments per patient varied: for hyperlipidemias it was 9.1 treatments per patients, for thrombotic thrombocytopenic purpura 8.2 treatments/patient, myasthenia gravis 5.6 treatments/patient, and Guillain–Barré syndrome 4.6 treatments/patient, with an overall average number of treatments per patient of 3.9. Treatment diagnosis also impacts the type of equipment used, while treatment reimbursement is impacted on by the payment provider. Plasmapheresis accounted for 60.1% of all reported treatments on 60.1% of all patients treated. These numbers represent a reduction from the prior survey (5). The largest total number of treatments were by plasma exchange (49.2%), followed by stem cell infu-

TABLE 21. *Response to apheresis and payment provider*

	Asia		Europe		Australia		North America		Central/South America		Total	
Type	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Response to apheresis												
Improvement	576	63.1	190	71.4	47	51.1	37	26.4	2	9.5	852	59.5
Same	70	7.7	50	18.8	21	22.8	94	67.1	1	4.8	236	16.5
Worsening	14	1.5	6	2.3	6	6.5	1	0.7	0	0.0	27	1.9
Treatment discontinued	11	1.2	12	4.5	5	5.4	2	1.4	1	4.8	31	2.2
Not assessable	242	26.5	8	3.0	13	14.1	6	4.3	17	81.0	286	20.0
(Total no. of patients)	(913)		(266)		(92)		(140)		(21)		(1432)	
Response to apheresis (above question) based upon:												
Subjective	76	11.2	45	21.4	13	14.1	2	1.4	3	75.0	139	12.4
Objective	120	17.8	48	22.9	12	13.0	13	9.4	0	0.0	193	17.2
Both	480	71.0	117	55.7	67	72.8	124	89.2	1	25.0	789	70.4
(Total no. of patients)	(676)		(210)		(92)		(139)		(4)		(1121)	
Payment provider												
Self/family	126	10.8	1	0.4	0	0.0	1	0.7	0	0.0	128	7.5
Private insurance	0	0.0	3	1.1	1	1.1	98	69.0	20	95.2	122	7.2
Government	762	65.1	149	53.4	82	93.2	40	28.2	1	4.8	1034	60.8
Hospital/institution	5	0.4	126	45.2	5	5.7	0	0.0	0	0.0	136	8.0
Other	278	23.7	0	0.0	0	0.0	3	2.1	0	0.0	281	16.5
(Total no. of patients)	(1171)		(279)		(88)		(142)		(21)		(1701)	

%, percentage of patients; *N*, number of patients.

sion (30.8%), and plasma treatment (10.9%). As in prior surveys, only a very small percentage of patients were treated by cytapheresis or lymphoplasmapheresis (3.5% in this survey).

Replacement solutions varied and are likely to be related to the disease state treated and the technology applied. Albumin solution was the most frequently used replacement solution, followed by fresh frozen plasma, and then electrolyte solutions. Plasma treatment by membrane (cascade) filtration and sorption treatments continue to be reported, but from only the Asian and European regions. Stem cell infusions were reportedly higher than first reported in the 2005 survey. For plasma sorption treatment, 72.7% of the treatments on patients were carried out with >10 treatments/patient, whereas for plasma exchange, stem cell infusions, and plasma treatment the majority of patients received 1–5 treatments. The treatment volumes on average for plasma exchange or plasma treatment were comparable (3.1 versus 2.7 L/treatment, respectively). While plasma treatment generally does not rely on plasma product replacements and the creation of a plasma product deficiency is less likely, it is curious that larger volumes of plasma were not treated. For whole blood adsorption the average volume treated was 7.8 L, more in line with the expectation of plasma processing with such a technology. Plasma treatment by membrane filtration was more predominantly practiced than sorption in this survey.

Central venous, peripheral veno-venous, and femoral vein blood access were the most common access methods. Citrate (47.9%), heparin and citrate (27.4%), and heparin (16.9%) were the most

TABLE 22. *Therapeutic apheresis procedures by country*

	Patients	Treatments	Population (million)	Cases/million inhabitants	No. of treatments/ million inhabitants
Canada	898	8 561	30	30.0	285
France	1021	10 700	60	17.0	178
Germany	–	6 941	82	–	85
Hungary	983	3 120	10	98.3	312
Italy	1477	15 205	58	25.5	262
Japan	–	11 697	127	–	92
Korea	1182	5 921	48	–	41–54
Philippines	194	735	83	2.3	9
Sweden	439	3 562	10	43.9	356
Turkey	172	869	67	2.6	13
USA	–	48 221	252	–	191
Venezuela	–	547	26	–	21

TABLE 23. *National view of therapeutic apheresis by frequency and disease*

	Reporting year	Population (million)	Cases	Procedures	Diseases by frequency	Diseases by number
Canada	2002	30	898	8 561	Hematological, neurological, vascular/renal	TTP, HUS, MG, macroglobulinemias
France	2003/04	60	942/1021	9 837/10 700	Hematological, neurological	TTP, HUS, FH
Germany	2002	82	–	6 941	GBS, cryoglobulinemia, MG, SLE, TTP	MG, GBS
Hungary	2001–2004	10	792–983	2 544–3120	Gammopathies, TTP, HUS	FH, SLE, cryoglobulinemia, GBS, MG
Italy	2000/1994–2004	58	2820/1477	15 202/15 285	GBS, cryoglobulinemia, MG, SLE, TTP	FH, SLE, cryoglobulinemia, GBS, MG
Japan	1995, 2002	127	–	11 697	FH, GBS, hepatic failure	FH, ulcerative colitis, malignant RA, fulminant hepatitis
Korea	2003–2006	48	1182	5 921	Hematological, metabolic, neurological	ABO incompatibility, TTP, MG, hyperviscosity, hepatic failure
Philippines	1994–2004	73–83	194	735	Neurological, hematological, renal/metabolic/ immunologic	Polyradiculoneuropathy, MG, TTP
USA	1991	252	–	48 221	GBS, leukemia, T-cell lymphoma	–
Venezuela	2003	26	–	547	–	–

FH, familial hypercholesterolemia; GBS, Guillain–Barré syndrome; HUS, hemolytic uremic syndrome; MG, myasthenia gravis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenic purpura.

common anticoagulants used. Regional differences exist, partly related to equipment type used (centrifugal versus membrane plasma separation), the location of the procedure (blood center versus dialysis center), and the choice of the physician in charge. Drug usage relates to the treatment diagnosis with 65.0% of patients not receiving steroids or immunosuppressive drugs, and 20.6% receiving steroids only. Equipment usage differences relate to regional equipment availability.

The most common side effect/complication was blood access difficulties, also with significant side effects/complications such as paresthesia, citrate-induced reactions, allergic reactions, hypertension, and hypocalcemia. Many of these are related to the use of citrate as the anticoagulant. One death was reported. In total, 1384 side effects/complications were noted in 6787 procedures reported, or 20.4% of the procedures.

The percentage of patients reportedly showing improvement was 59.5%, which is lower than that reported for 2005 of 74.8%, for 2002 of 78.8%, for 2000 of 73.1%, and for 1983 of 64.2%. A very high percentage, 20.0%, of the responses to apheresis was noted as not assessable in this survey. As in prior surveys, governments were reportedly the highest payment provider, and in this survey at 60.8% were down from 71.8% in 2005, 71.2% in 2002, 69.4% in 2000, and 30.8% in 1983. Regional differences are quite noteworthy and, in particular for the American regions, private insurances were the main payment provider. The differences among the reporting years in part relates to differences in regional reporting differences.

CONCLUSION

We can conclude, as noted also in prior years' surveys, that an international survey provides a broad perspective on the practices of apheresis, technologies and techniques applied, and clinical applications. This perspective is quite different than that of a national survey, which is very dependent on national clinical practices, reimbursement policies, and available technologies. Regional differences continue to exist related to local economics that dictate reimbursement policies and costs, disease treatment demographics, technology availability, physician training, education, and technical support.

Voluntary reporting continues to be the major impediment to data collection. Through an international survey a better understanding of the regional differences, whether related to economics, technology disease demographics, or other factors may contribute to a better understanding of apheresis practices that can lead to the development of better clinical practices worldwide.

Acknowledgements: This study was carried out under the auspices of the International Center for Artificial Organ and Transplantation (ICAOT) as part of its ongoing

TABLE 24. *National view of therapeutic apheresis by methods and side effects*

	Methods	Vascular access	Anticoagulation	Substitution fluids	Side effects
Canada	Centrifugation/PE	–	Citrate	Albumin/cryosupernatant plasma/FFP	12%, 0.4% severe
France	Centrifugation/plasma treatment	Peripheral vein	Citrate/heparin/LMWH	Albumin substitutes/ albumin/plasma	1.9%, 0.4% hypotension
Germany	–	–	–	–	–
Hungary	PE/cytapheresis	–	–	–	–
Italy	PE/cytapheresis/cascade filtration	AV fistula/central vein	Heparin/citrate	–	2.9–6.75%, 0.89% severe
Japan	Membrane filtration/ adsorption/centrifugation	–	Nafamostat mesilate/ heparin/LMWH/citrate	Crystalloids/albumin/FFP	21%
Korea	Centrifugation/filtration	Central vein/peripheral vein	Citrate	FFP/albumin	8.9%, 2.2% allergic, 1.8% hypotension
Philippines	PE	–	–	–	–
USA	Centrifugation/PE/platelet pheresis/photopheresis	–	–	–	–
Venezuela	Centrifugation/PE	–	–	–	–

AV, arteriovenous; FFP, fresh frozen plasma; LMWH, low molecular weight heparin; PE, plasma exchange.

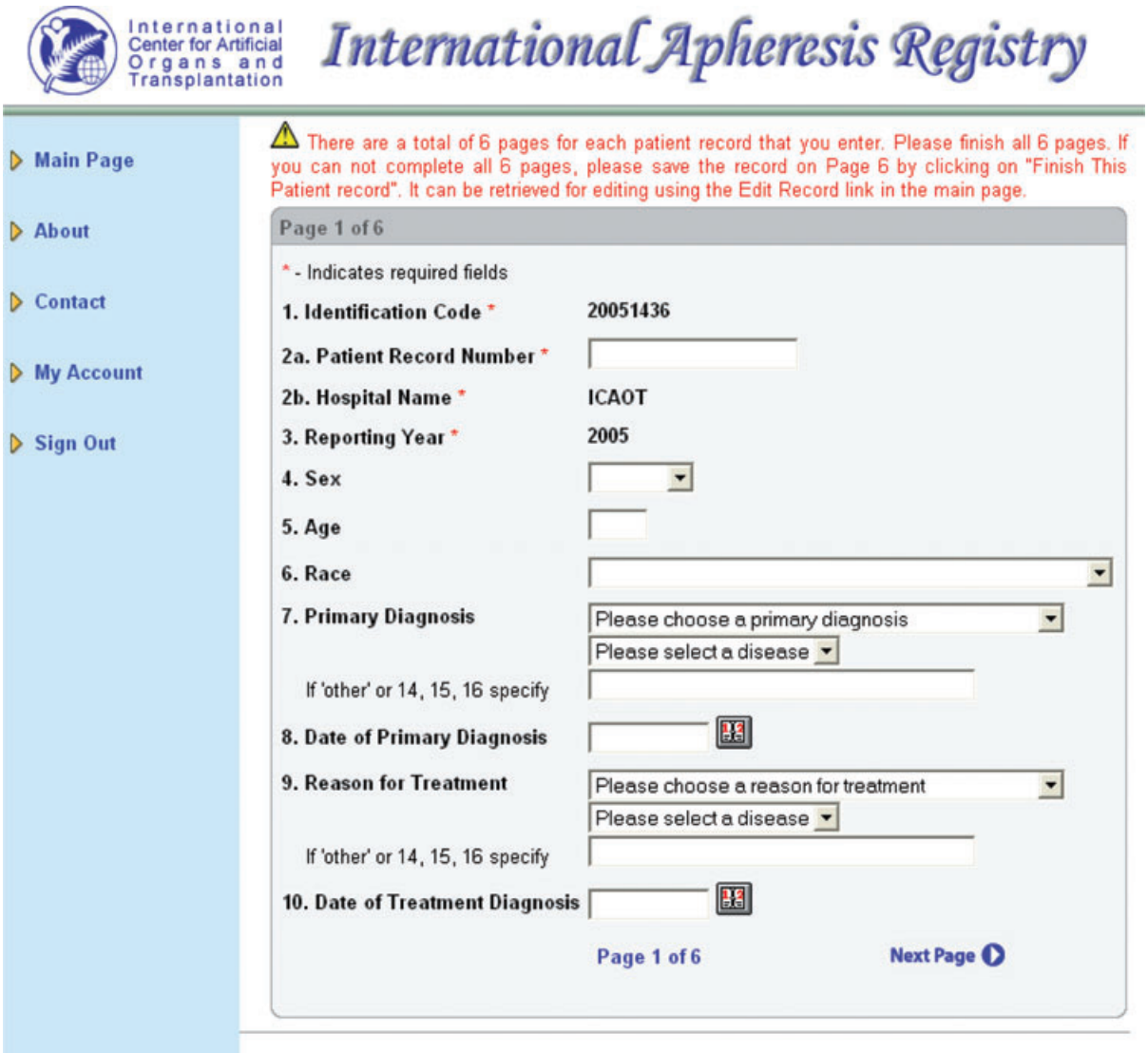
Technology Assessment Program and the International Society for Apheresis. The center and the authors are particularly thankful and indebted to those medical directors and institutions who so willingly participated in this survey (see Appendix II). We also especially thank the Department of Quantitative Health Sciences at the Cleveland Clinic for supporting this activity.

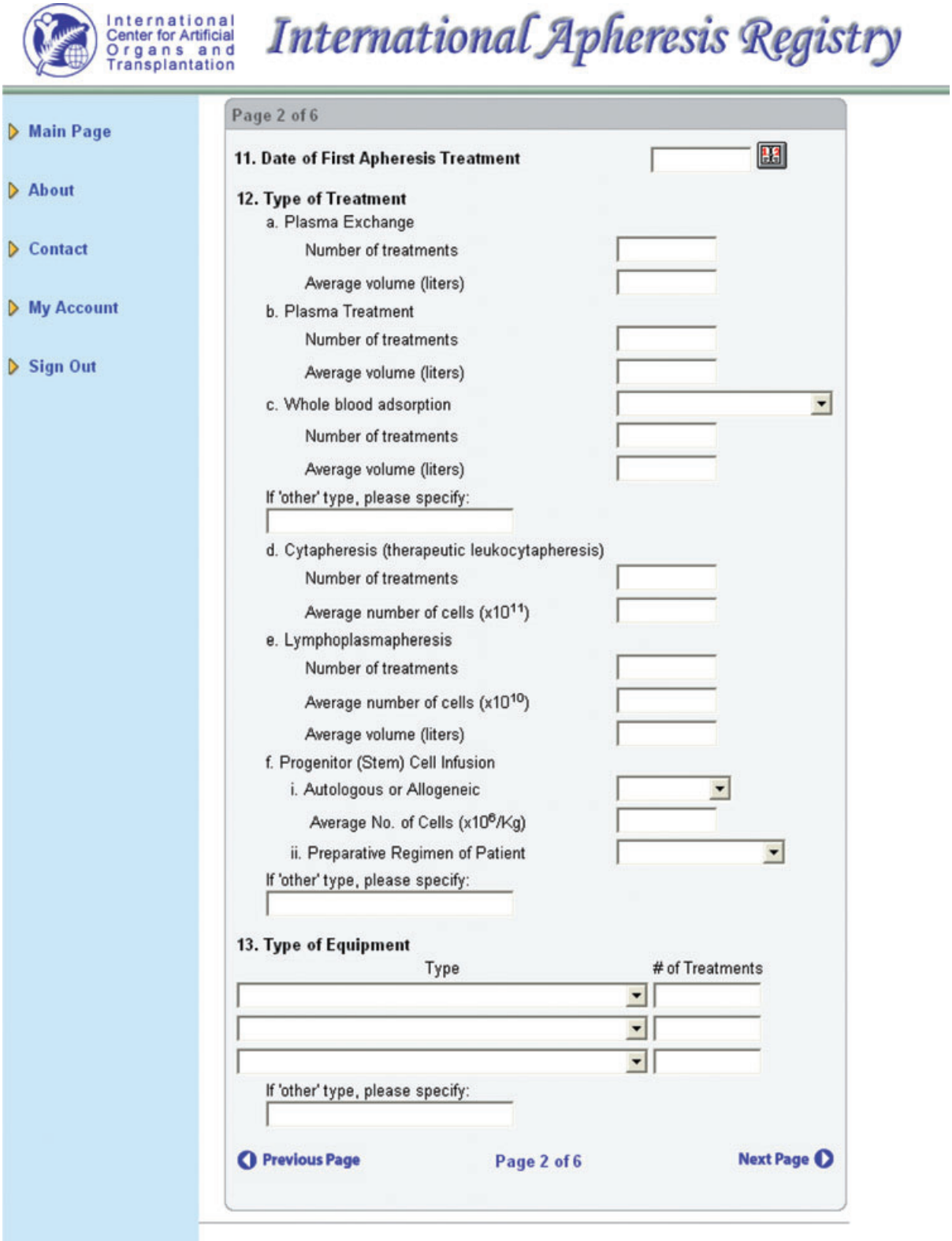
REFERENCES

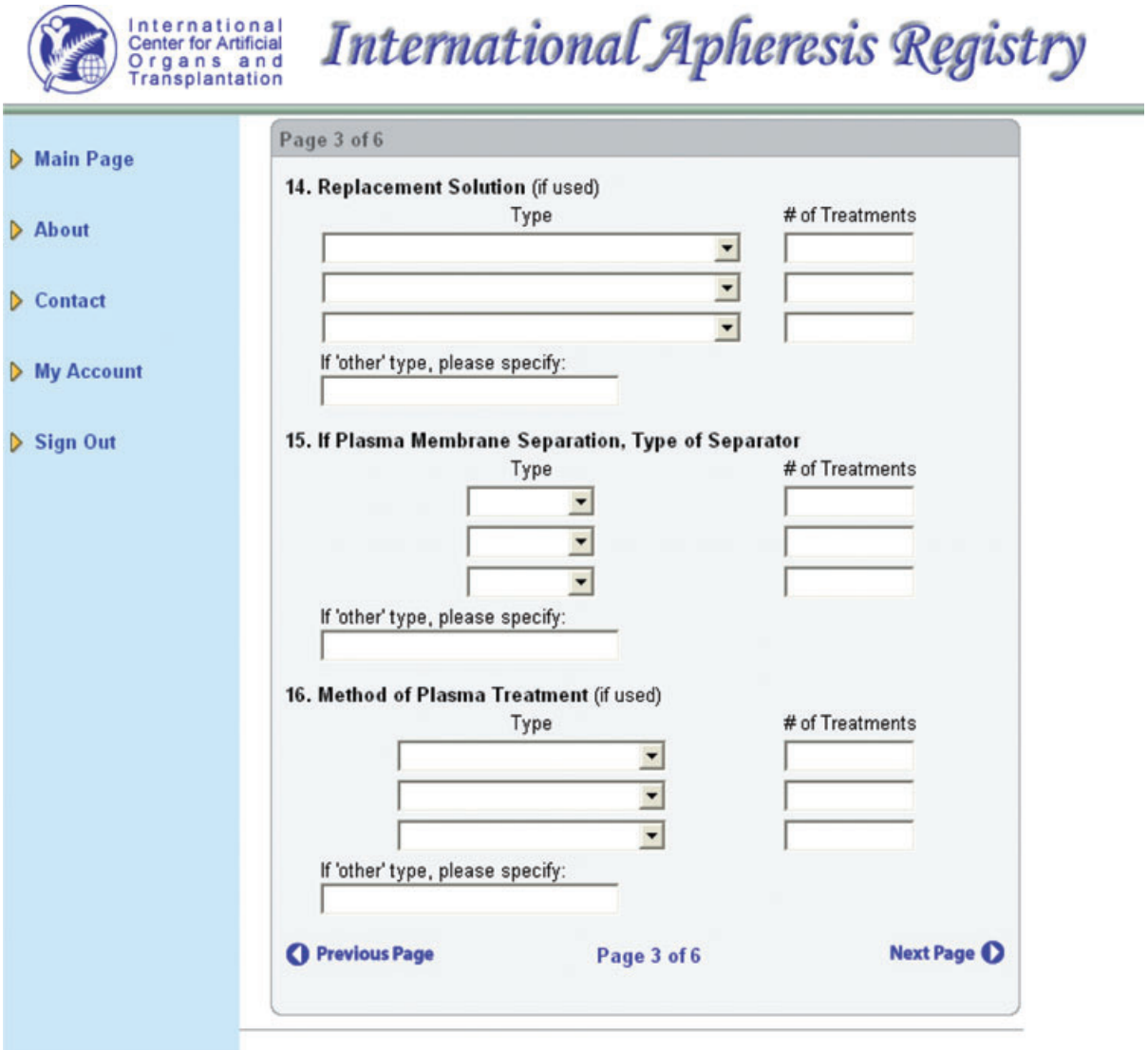
1. Malchesky PS, Skibinski CI, William GW, Nosé Y. The International Apheresis Registry: results of 1983 second pilot. *Artif Organs* 1987;11:173–82.
2. Malchesky PS, Skibinski CI. Summary of results of 1991ASFA apheresis survey. *J Clin Apher* 1993;8:96–101.
3. Malchesky PS, Koo AP, Rybicki LA. Apheresis technologies and clinical applications: the 2000 International Apheresis Registry. *Ther Apher* 2001;5:193–206.
4. Malchesky PS, Koo AP, Roberson GA, Hadsell AT, Rybicki LA. Apheresis technologies and clinical applications: the 2002 International Apheresis Registry. *Ther Apher Dial* 2004;8:124–43.
5. Malchesky PS, Koo AP, Roberson GA, Hadsell AT, Rybicki LA. Apheresis technologies and clinical applications: the 2005 International Apheresis Registry. *Ther Apher Dial* 2007;11: 341–62.
6. Malchesky PS, Leatherman JR, Nosé Y, Williams GW. The International Apheresis Registry: a progress report. In: Nosé Y, Malchesky PS, Smith JW, eds. *Therapeutic Apheresis: A Critical Look*. Cleveland, OH: ISAO Press, 1984; 61–7.
7. Stegmayr B, Ptak J, Wilkstrom B et al. World apheresis registry 2003–2007 data. *Transfus Apher Sci* 2008;39:247–54.
8. Rock G, Clark B, Sutton D, CAG; CAAN. The Canadian apheresis registry. *Transfus Apher Sci* 2003;29:167–77.
9. Korach J-M, for the French Registry Cooperative Group. French Apheresis Registry. Presented at World Apheresis Association Annual Congress held May 5–8, 2004, Miami, FL, USA. 2004.
10. Moog R. Haemapheresis activities in Germany. *Transfus Apher Sci* 2005;32:283–6.
11. Belak M, Jako J. National survey of hemapheresis practice in Hungary 2001–2004. *Ther Apher Dial* 2007;11:22–9.
12. De Silvestro G, Marson P, Russo GE, Vicarioto M, Donadel C. National survey of apheresis activity in Italy (2000). *Transfus Apher Sci* 2004;30:61–71.
13. Passalacqua S, Staffolani E, Busnach G et al. The Italian Registry for Therapeutic Apheresis. A report from the Apheresis Study Group of the Italian Society of Nephrology. *J Clin Apher* 2005;20:101–8.
14. Shimizu M, Tsuda H, Sanaka T, Ide K. Present status of therapeutic apheresis in Japan: survey report. (Survey Subcommittee, Scientific Committee, Japanese Society for Apheresis). *Ther Apher* 1998;2:172–81.
15. Scientific Committee of Japanese Society Apheresis. Tani T, Omokawa S, Koh CS, Sawada H, Takamori K, Mineshima M, Murabayashi S, Yokoyama H. Present status of apheresis in Japan. From the 2002 survey. *Jpn J Apher* 2005;24:110–18. In Japanese.
16. Song EY, Yoon JH, Lee JW et al. Establishment of a national on-line registry for apheresis in Korea. *Transfus Apher Sci* 2008;38:93–100.
17. Narciso CT. Therapeutic apheresis in the Philippines. *Transfus Apher Sci* 2005;33:3–9.
18. Kiprov DD. Delivery of therapeutic apheresis services in the United States. *J Clin Apher* 2005;20:123–5.
19. Saltiel C. Apheresis activity in Venezuela. *J Clin Apher* 2005; 20:95–100.

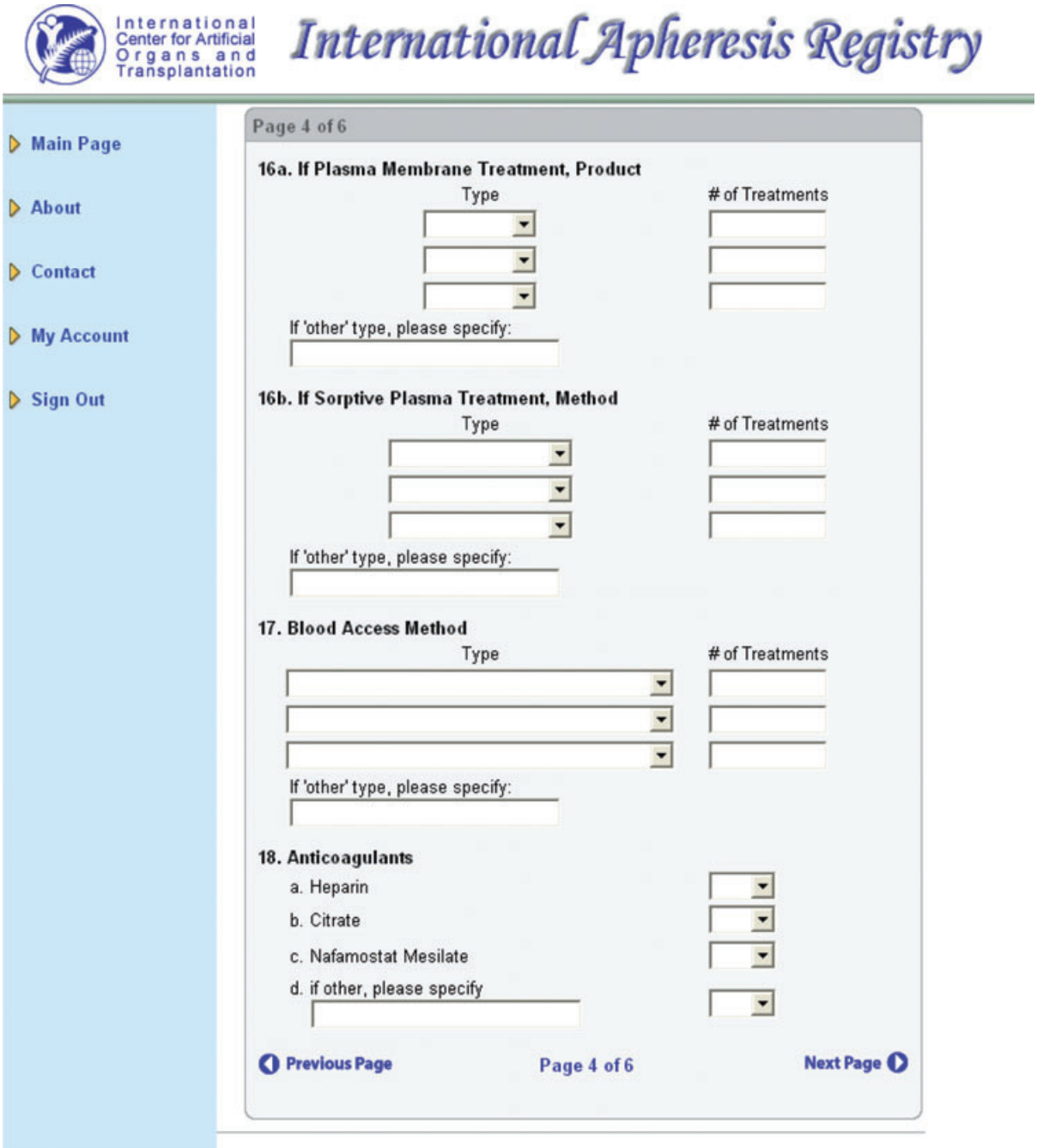
APPENDIX I

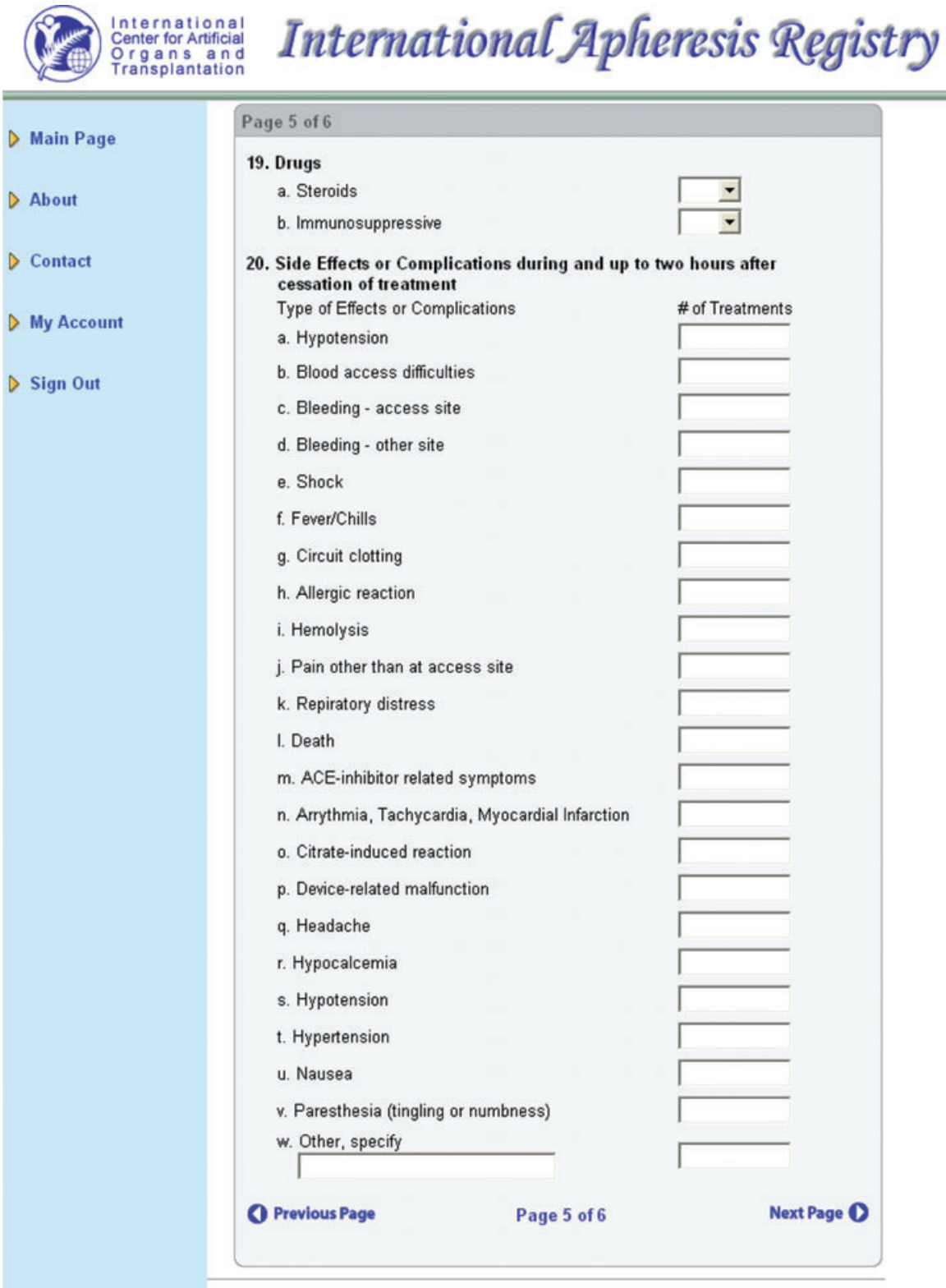
Online data entry forms for the 2007 International Apheresis Registry

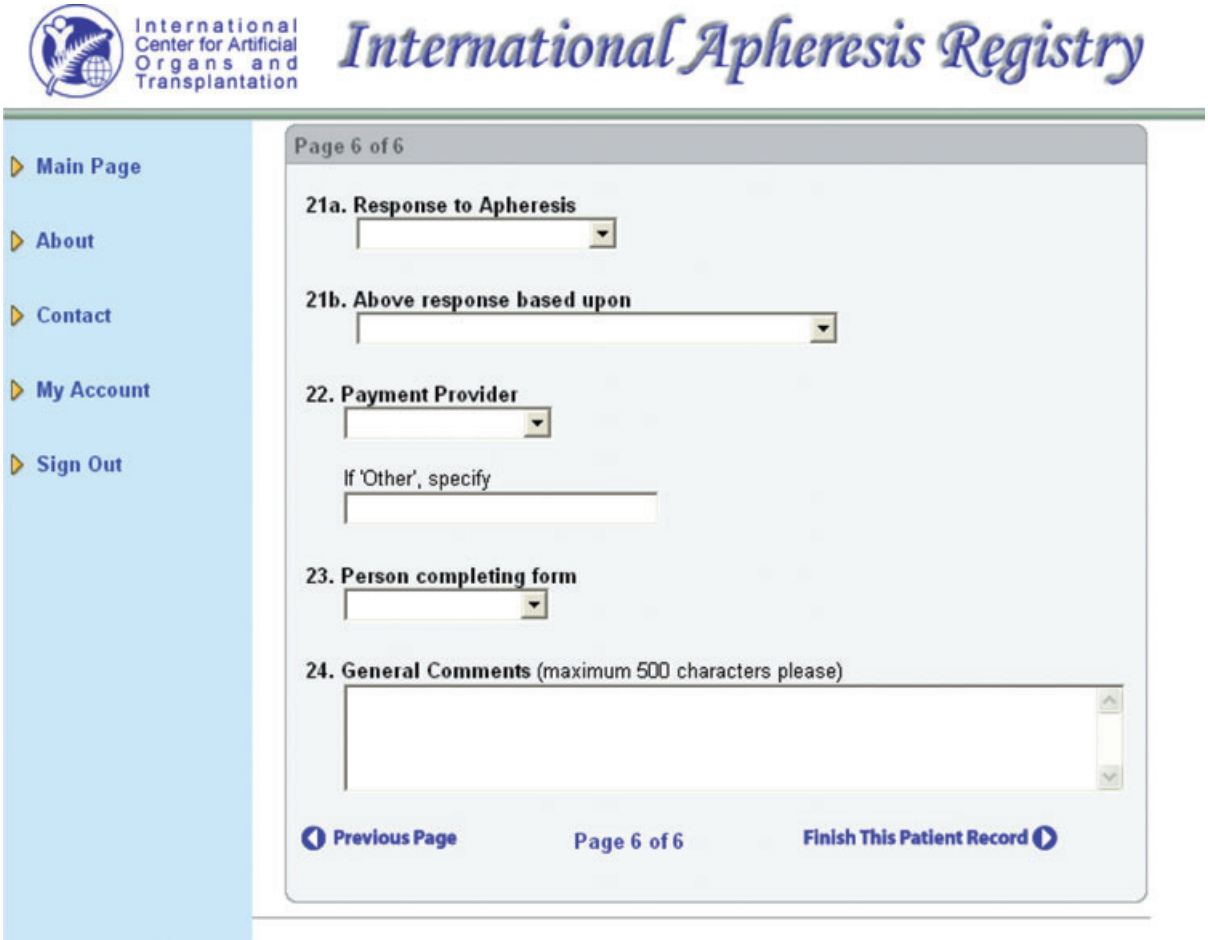












Appendix II

Collaborating persons and institutions

Participants	Department, Institution	City, Country
Meltum Bay	Ankara University School of Medicine	Ankara, Turkey
Wolfgang Ramlow, Heinrich Prophet, Anja Ramlow, Annett Bieber	Apheresis Center Rostock	Rostock, Germany
Ilknur Kozanoglu	Baskent University Medical Faculty	Ankara, Turkey
Anna P Koo	Cleveland Clinic	Cleveland, OH, USA
Elizabeth Newman, Lourdes Enriquez, Christine Fong, Pam Low	Concord Repatriation General Hospital	Concord, NSW, Australia
Birol Guvenc, Ferda Tekintuhan	Cukurova University Balcali Hospital	Adana, Turkey
Erini Grapsa, Nicolas Papaioanou, Konstantinos Pantelias, Maria Panagiotou, Stauroula Gerogiani	Alexandra Hospital Athens	Athens, Greece
Sergio Cabibbo, Pietro Bonomo, Agostino Antolino	Hospital "Civile-M.P. Arezzo"	Ragusa, Italy
Claudia Stefanutti, Serafina DiGiacomo	Hospital "Umberto I"	Rome, Italy
Norella C Kong	Hospital UKM	Kuala Lumpur, Malaysia
Omar A Trabadelo	Hospital Universitario Austral	Buenos Aires, Argentina
Rakesh Srivastava	ISA Institute for Apheresis and Research Center	Delhi, India
Phillip Wearden	Liverpool Hospital	Liverpool, NSW, Australia
Haekyoung Choung	Samsung Medical Center	Seoul, Korea
Ji-Weon Seo, Eun Young Song, Kyou-Sup Han, Yang Hyun Kim	Seoul National University Hospital	Seoul, Korea
Jiann-Horng Yeh, Hou-Chang Chiu, Mei-Fem Lee	Shin Kong Wu Ho-Su Memorial Hospital	Taipei, Taiwan
Petar Kes	University Hospital Center Zagreb	Zagreb, Croatia
Ljupco Stojkovski	University Nephrology Clinic – Skopje	Skopje, R. Macedonia
Gerda C Leitner	University Hospital Vienna	Vienna, Austria
Judita Audzijoniene, Antanas Griskevicius	Vilnius University Hospital, Santariskiu Clinics	Vilnius, Lithuania