Effect of Anesthesia on Hemostatic Mechanisms in Man

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RECENT investigations of coagulation during surgery have indicated that profound changes may occur following multiple transfusions.[1,2,3] A few reports have attempted to assess the effect of surgery itself on the coagulation system,[3,4] but little attention has been devoted to the possible role played by anesthesia.[5,6] In the present report, the effect of anesthetic agents, hypothermia and muscle relaxants on hemostatic mechanisms was investigated. The state of the hemostatic mechanism was appraised by a study of the activity of the coagulation factors in plasma, and the function of small blood vessels was measured by bleeding time and capillary resistance tests.

Material

Forty-one patients about to undergo surgery were studied. There were 18 males and 23 females, ranging from 9 to 80 years of age. Individuals with severe liver disease, coagulation defects, recent acute blood loss or chronic anemia were excluded.

Four groups of patients undergoing different anesthetic techniques were studied.

Eighteen patients received a single anesthetic agent: thiopental, 5 patients; diethyl ether, 3 patients; cyclopropane, 5 patients, and halothane, 5 patients.

Seven patients received a combination of anesthetic agents: thiopental and nitrous oxide, 3 patients, and diethyl ether and nitrous oxide, 4 patients.

Ten patients received a combination of anesthetic agents and a muscle relaxant: thiopental, nitrous oxide and *d*-tubocurarine, 3 patients, and thiopental, nitrous oxide and succinylcholine, 7 patients.

Six patients received anesthesia during induced hypothermia.

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Methods

Thiopental was administered intravenously as a 2.5 per cent solution by intermittent injection. Ether was given by the open-drop method. Cyclopropane anesthesia was induced with a semiclosed circle system using a 50 per cent mixture with oxygen and maintained with a closed circle system using the intermittent technique. Halothane was vaporized with 4 to 6 liters a minute of oxygen in a semiclosed circle system incorporating an Ohio Chemical Company Vernitrol vaporizer.

Nitrous oxide and oxygen, when given with thiopental, were initially administered at the rate of 4 liters a minute and one liter a minute respectively. After six to ten minutes the flow rate was reduced to 2 liters of nitrous oxide a minute and one liter of oxygen a minute. A semiclosed circle system with carbon dioxide absorption was employed throughout.

Nitrous oxide and oxygen, when used with ether, were initially administered at the rate of 4 liters a minute and one liter a minute until unconsciousness was produced. Sufficient ether vapor was added to produce a moderately deep level of anesthesia corresponding roughly to Stage III, plane 2, as described by Guedel.[7] The ether vapor concentration was then reduced to 2–3 per cent and the rate of flow of nitrous oxide and oxygen was reduced to 2 liters a minute and one liter a minute respectively. A semiclosed circle system with carbon dioxide absorption was employed.

Muscle relaxants were given by intermittent intravenous injection; *d*-tubocurarine in total doses of 6–30 mg., succinylcholine in total doses of 40–60 mg.

Hypothermia was induced and maintained with the aid of a refrigerant solution pumped through coil filled blankets placed above and

beneath the patients.* Occasionally icepacks were added to increase the speed of cooling. These patients were anesthetized with thiopental and nitrous oxide by the technique previously outlined. Small doses (3–9 mg.) of *d*-tubocurarine were used to control shivering.

Each of the laboratory tests listed below was carried out immediately prior to anesthesia and again approximately thirty minutes later after induction of anesthesia, but before the beginning of surgery. In hypothermic patients the tests were also made after cooling. A standard interval between collection of blood samples, bleeding time determinations and capillary resistance measurements was maintained for each anesthetic technique.

Clotting time, recalcification time, prothrombin consumption test, prothrombin activity (Quick), prothrombin activity (Owren), Factor V (labile factor) activity, proconvertin activity (Owren),† fibrinogen concentration and platelet count were determined by methods described in previous publications from this laboratory.[8,9] The thrombin time test was carried out with the use of a commercially prepared thrombin.‡ The clotting time of 0.2 ml. of plasma was determined at 37° C. after mixture with equal volumes of solutions containing thrombin in concentrations of 5 units/ml. and 50 units/ml. The thromboplastin generation test (TGT) was carried out by the method of Biggs and Douglas[10] with the following modifications: (1) Veronal buffered saline (VBIS) § was used to make all dilutions. (2) A soya bean phospholipid, asolectin # (20 mg./100 ml. VBIS) was substituted for a suspension of washed platelets. (3) Six-tenths milliliter each of asolectin, $Al(OH)_3$ adsorbed plasma (diluted 1:5), serum (diluted 1:10) and 0.025 *M* $CaCl_2$ were used to make the reaction mixture, of which 0.2 ml. was blown into 0.1 ml. substrate (platelet-poor plasma) at 9 and 12 minutes after initiation of the reaction mixture.

The percentage thromboplastin generation activity was calculated from reference curves prepared daily with serial dilutions of normal pooled $Al(OH)_3$ adsorbed plasma and of normal pooled serum.

The antihemophilic factor was assayed according to the method of Biggs[11] using the thromboplastin generation test as described above. For the purposes of this analysis a mixture consisting of 2 parts of $Al(OH)_3$ adsorbed hemophilic plasma and one part of $Al(OH)_3$ adsorbed normal plasma diluted five-fold with VBIS was considered as representing 100 per cent AHF activity. Serial dilutions of this mixture with a 1:5 diluted $Al(OH)_3$ adsorbed hemophilic plasma were made to prepare mixtures of decreasing AHF activity. A thromboplastin generation test with each of these mixtures was done daily and reference curves prepared from the 9 and 12-minute clotting times. Test plasmas were substituted for normal plasma in the plasma mixture and the AHF activity estimated from the thromboplastin generation time obtained.

The thromboplastin generation test was similarly adapted for assay of plasma thromboplastin component (PTC, Factor IX) by using dilutions of normal and test sera with serum from a patient with a severe congenital deficiency of PTC.

Bleeding time determinations were made by the Ivy method as modified by Jacobson[12] with the following refinements. A thin film of collodion was applied over an area approximately 1 × 3 cm. and allowed to dry. The use of a collodion film makes it possible to obtain a more definite end point since the blood does not adhere as closely as it does to skin, and can be more nearly completely removed by applications of filter paper made at 30 second intervals. The incisions were made with a no. 23A Bard Parker scalpel blade.** Each blade was protectively wrapped, placed in a small envelope, and ster-

* Thermo-O-Rite Products Company, Buffalo, New York.

† This test reflects the combined activity of Factor VII and Factor X.

‡ Fibrindex: Ortho Pharmaceutical Corp., Raritan, New Jersey.

§ Prepared by adding 200 ml. 0.1 *M* sodium barbital to 144 ml. 0.1 *N* HCl and adding 0.9 per cent NaCl to bring the final volume to 1000 ml., with a pH of 7.4.

Kindly supplied by Associated Concentrates Company, Long Island, New York.

** The no. 23A blade was prepared by the Bard Parker Company by grinding an edge on the back of the tip of a standard no. 23 blade, so that a triangular area 3 × 3 mm. was obtained, bearing a cutting surface on each of two sides.

ilized with ethylene oxide[13] to avoid the dulling of the cutting edge which occurs with other forms of sterilization. This modification of the blade was carried out in the interest of securing a cleanly incised wound. The use of a no. 11 Bard Parker blade in the standard bleeding time technique results in tearing of the tissues at the end of the wound opposite to the cutting edge, since such a blade has a wedge-shaped cross section. Incisions made with the no. 23A blade show an evenly incised aspect throughout. In addition, dimensional reproductibility is higher, because less force is required and there is no tearing or tissue rebound as is the case when one dull edge is presented. Direct measurements of the length of the incision on the same individual were repeatedly uniform. The blade was grasped with a hemostat, placed with its lower surface 3 mm. from the blade tip. This provided both a handle and a depth gauge. Two incisions, approximately 1 cm. apart were made. The incisions were placed at right angles to the long axis of the arm adjacent to the margin of the collodion film. The bleeding time for each incision was determined and the two averaged. Whenever there was a disparity of more than two minutes between the bleeding times of the two incisions, it was assumed that a large vessel had been severed by one of the incisions and the determination was repeated. In normal volunteers, the standard error of this method was 1.1 minutes for ten consecutive determinations on the same individual during a 45 minute period.

Capillary resistance was measured with a petechiometer as described by Scarborough,[14] modified †† as follows (fig. 1). To facilitate fine observation under the lens of the instrument a light source was added. This was made from a no. 2 Jackson bronchoscope bulb mounted in a detachable carrier and inserted into a hole drilled into the side of the transparent plastic cup. The power for this bulb was obtained from a Pilling E5705 detachable bronchoscope battery carrier, remotely located and connected to the petechiometer by wires.

†† This device, designed in collaboration with Mr. Carl Althausen, instrument maker to the Massachusetts General Hospital, was constructed under his supervision.

Vacuum was produced by a manually operated syringe pump (fig. 1). The plunger was threaded (4 threads per inch) to obtain a rapid rate of travel, yet permit the suction to be accurately produced and sustained. A pressure gauge mounted on the pump allowed constant observation of the degree of vacuum used and facilitated any necessary adjustment to maintain a predetermined figure. The pump was connected to the petechiometer cup by heavy walled rubber tubing, capable of withstanding negative pressures in excess of 500 mm. of mercury without collapse. The capillary resistance measurements were done on the skin overlying the pectoralis major rather than on the forearm. This area has been shown to yield the most reproducible results.[15] The rim of the petechiometer cup was coated with petroleum jelly to insure an airtight seal against the skin. At each pressure (increments of 25 mm. of mercury were used) two determinations were performed. The end point chosen was the least negative pressure necessary to produce two or more petechiae in the central portion of the viewing field.

Results

None of the agents tested produced consistent changes in any of the plasma coagulation factors. Certain patients exhibited moderately large changes in Factor V and prothrombin activity, but these variations are within the range of those often seen as a result of such nonspecific stimuli as multiple venipuncture or saline infusion.[16] In none of the cases in which a lowering of activity of a given factor after anesthesia was observed did the final values fall below the normal range.

There was a consistent but modest decrease in the mean values for capillary resistance with all agents. Eighteen of the 26 patients tested showed a decrease in capillary resistance (*i.e.*, increased capillary fragility). In 13 of the 18 cases, the fall was greater than twice the error of the method (table 1). In only one instance (patient 34, table 1), did the value reach a level sufficiently low to be considered of clinical importance; a decrease from 225 mm. of mercury before anesthesia to 25 mm. of mercury fifteen minutes follow-

ing the administration of thiopental, nitrous oxide and succinylcholine. This patient developed generalized petechiae, most marked over the skin of the trunk. She successfully underwent operation without undue hemorrhage, displaying both a rapid fading of the petechiae without development of new lesions, and spontaneous correction of the decreased capillary resistance to the preoperative level early in the postoperative period.

There were no impressive changes in the bleeding time except for marked elevations in two patients receiving halothane. In these patients (14 and 18) the bleeding time was 11 and 13 minutes following induction of anesthesia. Although this is greater than the range of normal for this test (3–6 minutes), no clinically detectable increase in bleeding resulted.

Disturbances in coagulation factors during hypothermia were minimal and similar to those seen during normothermia except for the greater depression of the mean values for plasma thromboplastin component and labile factor (table 2). Bleeding time was prolonged in all patients; remarkably so in some. Often the incisions made for this determination continued to ooze indefinitely (as was the case in patients 36 and 38 (table 1), recorded as 15+ and 17+ minutes) until the temperature returned towards normal, or until controlled by pressure. These prolonged bleeding times were not associated with an observable increase in hemorrhage in the surgical field.

Discussion

In view of the minimal disturbances observed during anesthesia at normal temperatures, it would seem that the contribution of any anesthetic agent or muscle relaxant to a significant alteration in hemostatic factors during surgery must be modest, if not negligible. The findings of slightly increased bleeding time and decreased capillary resistance in most cases probably resulted from the vasodilatation reported to be caused by most anesthetics.[17, 18, 19, 20]

The use of moderate hypothermia in anesthetized patients results in a somewhat greater, though still clinically unimportant, derangement of the hemostatic mechanism. However,

FIG. 1. Modification of Scarborough's petechiometer showing light with remote battery case, and syringe type vacuum pump.

during hypothermia the bleeding time became elevated to levels that could ordinarily be considered as dangerous and yet abnormal bleeding did not occur.

Indeed, no evidence of abnormal bleeding was encountered in any patient during the surgery which followed these studies. This forcefully points out that minor changes in the over-all pattern of hemostatic factors are rarely associated with unusual hemorrhage. It is probable that a gross deficiency of one factor or simultaneous reduction of several factors to very low levels is necessary to produce abnormal bleeding.

Summary

Examination of the hemostatic mechanism was performed in 41 patients during anesthesia at both normal and lowered temperatures. A variety of anesthetic agents and muscle relaxants, both singly and in combination, were employed. Both the mean values for the tests of coagulation and vascular factors before and after each anesthetic agent or combination of agents and the individual data for each patient studied are presented.

Only a few isolated changes of any magnitude were observed in normothermic patients. Little correlation with specific agents or tech-

TABLE 1

Hemostatic Mechanisms During Anesthesia. Results of Determinations on Individuals Patients

	Thiopental 5 Patients										Diethyl Ether 3 Patients						Cyclopropane 5 Patients									
	1		2		3		4		5		6		7		8		9		10		11		12		13	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Clotting Time (minutes)	19	17	19	18	17	14	16	18	18	18	17	22	17	16	12	14	16	17	22	20	14	13	21	17	16	13
Recalcification Time (seconds)	109	83	91	130	81	108	64	44	105	114	119	125	86	65	85	82	126	109	107	129	162	116	115	110	105	88
Thromboplastin (% of normal)	80	85	97	93	110	100	110	100	93	100	105	96	120	120	95	95	110	105	52	75	88	92	136	141	75	80
Antihemophilic Factor (% of normal)	55	65	97	109	135	118	129	133	100	100	100	106	115	125	110	103	113	110	122	129	100	102	132	132	86	86
Plasma Thromboplastin Component (% of normal)	100	105	90	110	132	108	100	108	136	133	115	115	90	85	115	107	84	84	92	81	75	75	112	100	111	110
Prothrombin Consumption (% of normal)	97	97	97	97	96	68		96	88	91	100	100	100	99	91	91	94	94	98	98	99	97	99	98	91	96
Prothrombin Time (Quick) (% of normal)	96	90	97	96	91	45	104	103	100	100	110	108	103	100	100	100	100	99	92	92	100	100	100	100	97	97
Prothrombin (% of normal)	94	104	135	135	140	110	116	116	102	108	127	127	107	107	100	100	96	96	115	115	120	120	88	80	89	89
Factor V (% of normal)	100	120	180	235	165	96	180	160	108	115	125	100	225	133	99	151	181	165	182	182	125	125	100	105	68	90
Proconvertin (% of normal)	84	91	108	98	150	120	111	109	80	73	225	170	153	103	82	88	115	113	130	108	110	117	75	74	40	50
Thrombin Time (50 U./ml.) (sec.)	3.8	3.7	3.3	3.3	3.8	4.0	4.2	4.8	3.5	3.5	3.4	3.4	4.0	4.2	3.6	3.6	3.3	3.8	3.8	3.8	3.5	3.5	2.8	3.1	3.2	3.1
Thrombin Time (5 U./ml.) (sec.)	12.6	12.3	11.9	11.9	13.5	14.4	14.0	14.7	10.8	11.0	12.6	12.8	13.4	13.6	15.0	15.0	12.5	13.4	12.3	12.3	13.6	13.6	10.8	12.6	14.2	13.4
Fibrinogen (grams)	.22	.20	.42	.39	.48	.43	.35	.35	.42	.47	.36	.44	.58	.61	.38	.39	.43	.39	.75	.61	.39	.30	.87	.93	.25	.30
Platelets ×1,000	309	316	225	232	260	260	187	176	103	160	318	337	521	535	353	372	249	245	554	558	454	431	170	184	235	278
Bleeding Time (minutes)	4	8.7	3.5	6.5	3.8	4	3.5	5.8	4.5	6.3	6	4.8	2.5	2.5	4	3.5	6	5	4	3	5.5	8.5	6.5	3.5	5	4.5
Capillary Resistance (mm. Hg)	200	125	275	250	250	225	200	125	75	50	400	350	400	400			75	125	125	100	275	150	300	250		

TABLE 1—*(continued)*

	Halothane 5 Patients										Thiopental and Nitrous Oxide 3 Patients						Diethyl Ether and Nitrous Oxide 4 Patients							
	14		15		16		17		18		19		20		21		22		23		24		25	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Clotting Time (minutes)	16	16	16	16	11	12	19	19	16	13	16	14	19	14	18	21	13	12	14	16	16	19	19	18
Recalcification Time (seconds)	64	64	53	47	36	41	86	102	83	82	91	93	97	133	60	105	103	68	91	90	76	68	50	95
Thromboplastin (% of normal)	109	112	100	110	100	105	105	100	55	50	94	91	43	48	43	42	33	33	90	95	105	108	122	122
Antihemophilic Factor (% of normal)	91	91	100	100	100	100	109	105	83	116	115	113	91	100	90	100	73	87	70	75	132	132	104	116
Plasma Thromboplastin Component (% of normal)	75	110	95	90	105	95	100	100	99	72	75	75	75	92	75	50	80	62	88	94	105	95	88	75
Prothrombin Consumption (% of normal)	97	93	91	93	97	97	95	93	98	98	97	95	98	98	100	100	94	88	98	97	100	100	100	99
Prothrombin Time (Quick) (% of normal)	116	103	122	101	115	112	70	78	103	90	115	115	98	98	90	90	92	92	112	112	113	110	100	102
Prothrombin (% of normal)	92	90	105	105	107	107	105	96	100	100	95	99	100	100	84	93	90	90	100	100	112	200	88	92
Factor V (% of normal)	128	130	142	132	140	135	180	82	100	105	140	140	92	90	100	90	115	80	48	42	100	180	100	84
Proconvertin (% of normal)	125	100	113	110	105	107	98	96	92	100	68	68	113	105	77	80	65	21	145	100	235	275	135	145
Thrombin Time (50 U./ml.) (sec.)	4.3	4.2	4.0	3.9	3.3	3.5	3.2	3.5	4.0	3.0	4.2	4.1	3.2	3.5	2.8	3.0	3.0	2.9	3.7	4.3	3.4	3.3	3.2	3.4
Thrombin Time (5 U./ml.) (sec.)	12.8	12.8	12.1	12.3	12.1	12.0	12.7	13.5	15.0	12.2	13.5	13.8	12.5	12.3	11.4	11.5	14	12.9	12.7	13.8	12.7	12.6	12.7	12.2
Fibrinogen (grams)	.28	.26	.47	.42	.56	.55	.58	.63	.45	.58	.30	.43	.44	.42	.64	.57	.58	.62	.27	.23	.58	.60	.41	.65
Platelets ×1,000	238	229	403	392	653	668	211	190	275	280	247	240	238	234	470	480	268	265	280	303	322	345	325	330
Bleeding Time (minutes)	5.3	10.8	4.5	4.8	4.3	6.3	2.3	4.3	5.3	12.8	6	5.3		6.3	3.5	3.3	4	4.5	3.5		8.5	9.3	6	3.5
Capillary Resistance (mm. Hg)	125	100	125	50	200	200	100	50			275	200		150	175	175			225		200	125	125	150

TABLE 1. (*Continued*)

Hemostatic Mechanisms During Anesthesia. Results of Determinations on Individual Patients

	Thiopental, Nitrous Oxide and *d*-Tubocurarine 3 Patients						Thiopental, Nitrous Oxide and Succinylcholine 7 Patients												Induced Hypothermia 6 Patients											
	26		27		28		29		30		31		32		33		34		35		36		37		38		39		40		41	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Clotting Time (minutes)	16	8	23	21	16	18	10	16	20	17	18	16	19	18	21	16	13	14	15	16	15	17	10	12	16	15	16	13	18	11	17	21
Recalcification Time (seconds)	142	97	125	102	58	55	110	90	90	77	91	95	114	97	83	50	102	90	69	62	67	53	117	112	231	85	95	163	58	44	111	99
Thromboplastin (% of normal)	99	69	120	120	107	110	120	100	105	105	52	70	105	80	75	102	100	100	62	82	92	88	130	43	39	27	70	48	150	80	100	81
Antihemophilic Factor (% of normal)	88	57	120	134	112	116	75	75	134	134	60	60	100	124			140	130	104	120	100	88	100	157	94	94	60	60	110	100	75	90
Plasma Thromboplastin Component (% of normal)	108	83	100	88	90	75	98	98	110	118	23	23	90	100			100	100	95	95	45	50	80	70	72	14	23	12	100	112	100	100
Prothrombin Consumption (% of normal)	96	100	97	98	96	87	98	96	100	97	97	96	99	96	98	96	99	97	98	98	96	95	96	96	95	97	90	95	94	97	97	95
Prothrombin Time (Quick) (% of normal)	107	102	117	115	125	125	137	130	101	100	77	77	100	88	120	120	115	108	111	109	78	87	135	74	78	88	86	64	102	94	175	145
Prothrombin (% of normal)	117	117	142	130	125	128	200	270	86	84	64	64	88	80	100	107	100	100	160	160	100	100	100	75	80	88	64	59	115	117	99	99
Factor V (% of normal)	132	120	100	90	140	110	155	200	92	80	135	110	150	155	98	130	210	220	135	135	83	83	91	53	60	58	77	48	102	99	100	64
Proconvertin (% of normal)	120	105	100	100	240	205	140	138	235	145	85	86	64	60	90	140	100	91	99	122	92	107	100	48	53	49	110	120	220	218	136	128
Thrombin Time (50 U./ml.) (sec.)	4.0	3.4	3.4	3.5	4.2	4.2	2.8	2.8	3.2	3.2	3.8	4.1	3.1	3.8	3.8	3.5	3.7	3.8	2.8	3.7	3.7	3.4	3.7	4.1	3.9	3.7	4.1	4.9	4.0	3.3	4.0	3.4
Thrombin Time (5 U./ml.) (sec.)	13.2	13.4	11.5	11.7	13.5	13.8	12.2	12.2	13.1	13.2	13.0	13.4	12.6	13.5	12.4	12.4	11.5	12.2	13.2	11.8	12.4	12.2	12.8	11.0	12.4	12.0	13.4	23.8	12.4	12.8	12.1	14.1
Fibrinogen (grams)	.8	.6	.4	.41	.4	.37	1.0	.8	.56	.51	.34	.30	.78	.71	.41	.43	.40	.45	1.0	1.1	.32	.35	.47	.31			.30	.36	.81	.83	.34	.38
Platelets ×1,000	228	198	372	336	209	205	220	230	273	297	209	196	505	510	230	233	253	275	500	497	197	189	162	386	221	230	196	183	380	401	344	368
Bleeding Time (minutes)	5	5	3.5	3.3	3.3	5	4.5	5.8	3.3	4.3	3.8	4.5	4.8	4	8.8	9.3	5	6.8	3	2	2.5	15+		13.5	5.5	17+	4.5	9.8	5.5	8.5	5.3	
Capillary Resistance (mm. Hg)			350	350	250	150			75	225	225	250	250	200	150	50	225	25			225	300	125	125	225	175	250		200	250	275	450

TABLE 2. Mean Values for Congulation Tests During Anesthesia

	Cyclopropane 5 Patients		Thiopental 5 Patients		Thiopental and Nitrous Oxide 3 Patients		Thiopental, Nitrous Oxide and *d*-Tubocurarine 3 Patients		Thiopental, Nitrous Oxide and Succinylcholine 7 Patients		Ether 3 Patients		Halothane 5 Patients		Nitrous Oxide and Ether 4 Patients		Hypothermia 6 Patients		Standard Error of Method
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	
Clotting Time (minutes)	17.8	16.0	17.8	17.0	17.0	16.3	18.3	16.0	17.4	16	15.0	17.3	15.0	15.2	15.5	16.3	15.3	14.8	.48
Recalcification Time (seconds)	123	100	90	90	83	110	108	91	91	81	97	91	95	97	80	80	113	93	3.6
Thromboplastin (% of normal)	92	99	99	97	60	60	109	99	88	93	107	104	94	97	89	90	97	91	18.0
Antihemophilic Factor (% of normal)	111	112	103	105	100	104	107	96	102	107	108	111	97	102	95	103	101	98	7.8
Plasma Thromboplastin Component (% of normal)	95	91	112	113	72	67	96	82	86	97	107	102	95	95	93	82	70	61	4.0
Prothrombin Consumption (% of normal)	96	96	95	90	90	95	96	95	96	96	97	97	96	95	98	99	96	96	1.29
Prothrombin Time (Quick) (% of normal)	98	98	98	87	101	101	116	114	102	104	104	103	107	97	104	104	109	92	9.5
Prothrombin (% of normal)	102	99	117	115	93	97	128	127	114	124	111	111	102	100	98	121	93	90	4.4
Factor V (% of normal)	149	157	147	145	110	109	124	109	139	147	150	128	138	117	113	98	86	68	2.0
Proconvertin (% of normal)	94	94	107	101	86	84	153	136	129	112	153	120	107	101	145	135	119	112	2.8
Thrombin Time (50 U./ml.) (sec.)	3.3	3.5	3.7	3.9	3.4	3.5	3.9	3.7	3.3	3.5	3.7	3.7	3.8	3.6	3.3	3.5	3.9	3.8	0.4
Thrombin Time (5 U./ml.) (sec.)	12.7	13.1	12.6	12.9	12.3	15.9	12.7	12.9	12.6	12.7	13.7	13.8	12.9	12.6	13.0	12.3	12.6	14.8	0.17
Fibrinogen (grams)	.54	.51	.38	.37	.48	.47	.53	.46	.65	.61	.44	.48	.47	.49	.46	.53	.45	.45	.01
Platelets X1,000	332	339	229	229	318	318	267	246	313	320	307	415	356	352	266	311	251	293	28.3
Bleeding Time (minutes)	5.5	4.9	3.8	5.6	5.3	4.9	3.8	4.7	4.6	5.7	3.9	3.6	4.3	7.8	5.6	5.9	5.9	12.8	1.1
Capillary Resistance (mm. Hg)	155	125	200	155	223	175	300	250	185	150	400	375	110	80	182	138	267	260	25

niques employed for anesthesia was observed. During hypothermia some patients showed slight to moderate disturbances in some plasma coagulation factors and the bleeding time was prolonged in all patients. There were no instances of abnormal hemorrhage.

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