Therapeutic Apheresis
1(1):83–108, Blackwell Science, Inc., Boston

Historical Perspective on Plasmapheresis

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PLASMAPHERESIS

Plasmapheresis is derived from a Greek word meaning to take away by force. The term was first used by Abel in 1914 in his report entitled, "Plasma removal with return of corpuscles (plasmapheresis)" wherein he reported that large amounts of plasma could be collected from an animal if the red blood cells were returned (Figs. 1 and 2). It is only within the past twenty-five years that this term has come into prominence.

Today, plasmapheresis is the separation of plasma from the cellular components of blood with the cells being returned to the patient. The primary use of this procedure is in the collection of normal plasma for fractionation. Plasmapheresis is also employed for therapeutic use. A recent "state of the art" article cites over 50 diseases treated by plasmapheresis worldwide (1). Tables 1–8 reprinted from this paper identify the various disease states, the variety of procedures, sorbents, membrane filters currently used and the relevant features of membrane and centrifugal plasma separation systems.

The recent progress in plasma separation and plasma treatment technologies has provided a powerful tool in therapeutic medicine for diseases that were once considered difficult to treat by conventional methods (2–10).

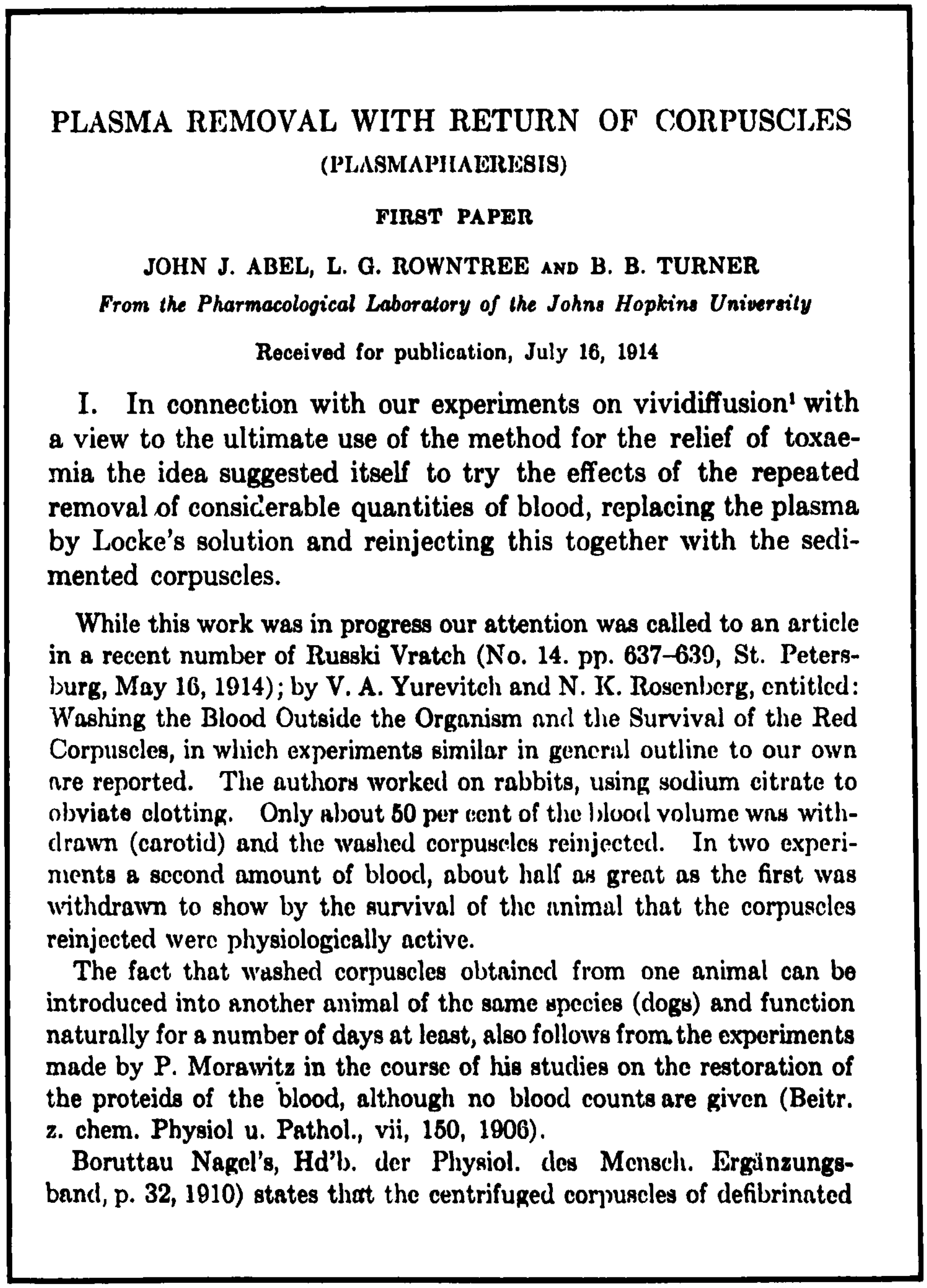
The therapeutic application of plasma separation includes two general techniques: *plasma exchange* and *plasma perfusion* (1). In plasma exchange, a volume of plasma is removed and replaced with an equivalent volume of plasma or plasma substitute. In plasma perfusion, after the plasma has been separated from the cellular elements, it is treated either by absorptive columns or filtration to remove the unwanted plasma components. The treated plasma is then returned to the patient.

BLOODLETTING

Bloodletting, the therapeutic removal of blood from the body, has been performed as a remedy for almost every illness known to man in nearly every society and culture of the world. As the theories surrounding the procedure grew more complex so did the devices used to perform the technique. Since its origin, the practice of bloodletting has been marked by controversy, but proponents were quick to emphasize that at the time little else could be offered as a remedy for disease.

In the early 18th century bloodletting and related procedures reached their height in popularity. With

FIG. 1. John J. Abel (from Alan Mason Chesney Medical Archives, the Johns Hopkins Medical Institutions, with permission).



PLASMA REMOVAL WITH RETURN OF CORPUSCLES
(PLASMAPHAERESIS)

FIRST PAPER

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From the Pharmacological Laboratory of the Johns Hopkins University

Received for publication, July 16, 1914

I. In connection with our experiments on vividiffusion[1] with a view to the ultimate use of the method for the relief of toxaemia the idea suggested itself to try the effects of the repeated removal of considerable quantities of blood, replacing the plasma by Locke's solution and reinjecting this together with the sedimented corpuscles.

While this work was in progress our attention was called to an article in a recent number of Russki Vratch (No. 14. pp. 637–639, St. Petersburg, May 16, 1914); by V. A. Yurevitch and N. K. Rosenberg, entitled: Washing the Blood Outside the Organism and the Survival of the Red Corpuscles, in which experiments similar in general outline to our own are reported. The authors worked on rabbits, using sodium citrate to obviate clotting. Only about 50 per cent of the blood volume was withdrawn (carotid) and the washed corpuscles reinjected. In two experiments a second amount of blood, about half as great as the first was withdrawn to show by the survival of the animal that the corpuscles reinjected were physiologically active.

The fact that washed corpuscles obtained from one animal can be introduced into another animal of the same species (dogs) and function naturally for a number of days at least, also follows from the experiments made by P. Morawitz in the course of his studies on the restoration of the proteids of the blood, although no blood counts are given (Beitr. z. chem. Physiol u. Pathol., vii, 150, 1906).

Boruttau Nagel's, Hd'b. der Physiol. des Mensch. Ergänzungsband, p. 32, 1910) states that the centrifuged corpuscles of defibrinated

FIG. 2. Introduction to the article on plasmapheresis published by Abel, Rountree, and Turner in the *J Pharmacol Exp Ther*, 5:625–641, 1914.

the increased knowledge of anatomy and hematology, bloodletting began to decline in the Western world by the middle of the 19th century.

The practice of plasmapheresis should not be confused with classical bloodletting. The two therapies spring from entirely different theoretical bases and are used to treat different conditions. But plasmapheresis, because it involves the removal of plasma from the blood, does call to mind the ancient practice of bloodletting (Fig. 3).

The Egyptians were known to take blood baths to restore health and to maintain youthfulness. When they saw an animal rub against a tree until its leg bled, they claimed it was the animal's way of removing excess blood from its body; therefore, they believed in the use of therapeutic bloodletting for themselves (Fig. 4).

The art of medicine in the ancient world developed to its highest point in Greece, during the millenium between 500 B.C. and 500 A.D. This creative period is symbolized by Hippocrates, the "Father of Medicine," whose name has come to represent the

TABLE 1. *Kinds of procedures in therapeutic apheresis*

Procedure	Method
I. Plasma exchange (plasmapheresis for plasma separation)	Centrifugal method (manual intermittent, automated continuous) Membrane method (TMP of plasma flow controlled, rotating filter system)
II. On-line plasma fractionation	Membrane method
1. On-line membrane plasma fractionation[a]	
a. Cascade filtration (double filtration plasmapheresis)	
b. Cryofiltration	
c. Thermofiltration	
2. On-line sorption plasma fraction[a] Sorbent	Biological sorbent (protein A column, immunoadsorbent IM-TR, etc.) Nonbiological sorbent (resin, activated carbon, etc.)
3. Others Precipitation	
III. Cytapheresis	Methods include centrifugal, select cell removal filter, and photopheresis
a. Leukocytapheresis	
b. Plateletapheresis	
c. Erythrocytapheresis	
IV. Leukoplasmapheresis	Centrifugal method

[a] Membrane method is preferred as the plasma separator since the separated plasma is free of cells.

beauty, value, and dignity of medicine for all times. Hippocrates' kindliness and concern are embodied in his aphorism, "Where there is love for mankind, there is love for the art of healing." It was Hippocrates (460–377 B.C.) to whom the introduction of bloodletting as a preventive method as well as a remedy could be ascribed (Figs. 5–7).

Galen was a pillar of medicine; the last important pillar in the millennium of Greek domination of the medical world. Physician to emperors as well as commoners in the Roman Empire, Galen (130–211 A.D.) traveled extensively, lectured widely, and wrote prolifically. The great Greek was a shrewd observer who gained much experience through experimentation. Cupping was among the forms of treatment he advocated. Pharmacy as well as medicine benefited from his formulas, called "galenicals." He was a leader in the health sciences of his day. Galen's teachings were accepted as dogma by both teachers and practitioners of medicine for fifteen hundred years (Fig. 8).

Galen's reasoning for the support of bloodletting and cupping was the "humoral theory" which proposed that illness was caused by an imbalance of the body's four humors: blood, yellow bile, black bile, and phlegm. Once the humors were balanced through the removal of blood, then the individual was restored to health. "Bad humors" were thought to be responsible for ill health and emotional states such as depression and insanity (Fig. 9).

During the Middle Ages (500–1500 A.D.), therapeutic techniques dealing with blood were frequently done by barber–surgeons who took over procedures shunned by surgeons. Barbers commonly practiced bleeding, cupping, and leeching along with their more conventional tasks.

The barber–surgeons of the 15th century were known to place a striped pole or a signboard outside their doors to distinguish their practice from that of the surgeons. From the signboard there was usually hanging a basin which was used to catch the drained blood.

The barber's pole, which is still evident today, is a symbol from medieval times. The poles represented the stick which was grasped by the patient to promote bleeding. The white stripe represented the tourniquet which was tied just above the vein to be opened, and the red stripe represented the blood as it flowed down the arm of the patient (Fig. 10).

Special bowls to catch the blood as it flowed from a vein were made for the first time in the 14th century (Fig. 11). The earlier basins were made of clay or brass, and later pewter bowls were made. Some of the pewter bowls had gradations to measure the amount of blood removed. There was a variety of pewter bowls used between the 17th and 19th centuries (Fig. 12).

The earliest cutting instruments for bloodletting were fish teeth and sharp stones. The thumb lancet was developed during the 15th century. It had a double edge connected to two sheaths which served as a cover and were usually made out of shell or horn.

The fleams were used in the 17th and 18th centu-

TABLE 2. *Disease states for which plasmapheresis has been reportedly applied*

	Classification			
	I. Abnormal protein-related disease		II. Autoimmune antibody-related disease	III. Immune complex-related disease
Collagen and rheumatological disease	Raynaud's disease:	Cryoglobulin Macroglobulin	SLE: anti-DNA Ab, ANA, (IgG, M, A), anti-Sm Ab, anti-Ku Ab, anti-PCNA Ab	SLE
	RA:	Cryoglobulin	RA: RF (IgM), anti-RANA Ab	RA
			PSS: anti-nonhistone nuclear Ab	PSS
			Scleroderma: anti-Og (Scl-70) Ab, (70,000)	Scleroderma
			MCTD: anti-U_1 snRNP Ab, ANA, anti-Sm Ab, ENA, RF	
			CREST syndrome: anti-centromere Ab	
			Sjögren syndrome: anti-SSA Ab, anti-mitochondria Ab, anti-SSBAb (LaAb, HaAb), ENA, ANA	
	PN:	Cryoglobulin Macroglobulin	Overlap syndrome (PSS and PM): anti-Ku Ab	
			PN: RF	PN (HBsAg Ab immune complexes)
Neurological diseases	MG:	Cryoglobulin	MG: anti-Ach R, Ab, anti-SM Ab (IgG 1, 2, 3) anti-skeletal muscle Ab	
			MS: anti-myelin Ab	
			GBS: anti-myelin Ab, anti-SP-B8-Ab	GBS
	Polyneuropathy:	Cryoglobulin Macroglobulin	PM and DM: anti-Jo 1 (Ab, anti-PM-Scl Ab)	
			Polyradiculoneuropathy: anti-SP-B Ab	
Liver disease	Fulmimant hepatitis:	Protein-bound toxins	Chronic active hepatitis: anti-mitochondrial Ab	
	Hepatic failure:	Protein-bound toxins		
	PBC:	Protein-bound toxins	PBC: anti-mitochondrial Ab	
Hematological disease	Paraproteinemia:	Paraprotein	ITP: anti-platelet Ab (IgG)	
	Macroglobulinemia: (hyperviscosity syndrome)	Macroglobulin (IgM) (900,000)	TTP: anti-platelet Ab (IgG)?	TTP
			Autoimmune hemophilia A: anti-factor VIII Ab	
	Cryoglobulinemia:	Cryoglobulin	Preparation for ABO incompatible marrow transplantation: anti-A or B Ab	Schönlein-Henoch purpura
			RH incompatibility: anti-Rh Ab	
			Autoimmune hemolytic anemia: anti-red cell Ab, cold-hemolysin (IgG), cold-hemaglutinin (IgM)	
			Pernicious anemia: intrinsic factor Ab (IgG, M, A)	
	AIDS:	Suppressor factors?	AIDS: anti-lymphocyte Ab	AIDS
Renal diseases			Anti-glomerular basement membrane (GEM) mediated glomerulonephritis: anti-GBM glomerulonephritis (IgG, M, A)	Immune complex glomerulonephritis
			Goodpasture's syndrome: anti-glomerular basement membrane Ab	
			Rejection of kidney transplantation: anti-HLA Ab	Rejection of kidney transplant
Malignant diseases	Cancer:	CA19-9 (820,000), α_2 MG (820,000), CEA (200,000), AFP (70,000), IAP (57,000), etc.	Cancer: tumor-specific antibody	Cancer
	Multiple myeloma:	M-protein (IgG, M, A, E)		
Others	Hyperlipidemia: Familial hypercholesterolemia)	LDL, VLDL	DM I-B type: anti-insulin receptor Ab	
			Insulin autoimmune syndrome: anti-insulin Ab (IgG, A)	
			Asthma: IgE	
	Toxins		Urticaria: IgE	
	Poisons		Ulcerative colitis: anti-colonic lipopolysaccharide	
			Basedow's disease (Graves' disease): LATS (IgG)	
			Autoimmune thyroiditis: anti-microsomal Ab	
			(Hashimoto's disease): anti-thyroglobulin Ab	
			Addison's disease: anti-adrenal Ab (IgG)	
			Autoimmune chronic atrophic gastritis: parietal cell Ab (IgG, M, A)	
			Chronic ulcerative colitis: anti-colonic epithelial cell Ab	
			Pemphigus: anti-epidermal cell membrane glycoproteins Ab	

SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; PSS, progressive systemic sclerosis; MCTD, mixed connective tissue disease; PN, periarteritis nodosa; MG, myasthenia gravis; MS, multiple sclerosis; GBS, Guillain-Barré syndrome; PM and DMS, polymyositis and dermatomyositis; PBC, primary biliary cirrhosis; ITP, idiopathic thrombocytopenia purpura; TTP, thrombotic thrombocytopenic purpura; DM, diabetes mellitus; AIDS, acquired immunodeficiency syndrome; ENA, anti-extractable nuclear antibody; RNP, ribonucleoprotein; ANA, anti-nuclear Ab; HLA, human leukocyte antigen; LATS, long-acting thyroid stimulator; Ab, antibody; RF, rheumatoid factor, RANA, rheumatoid-associated nuclear antigen.

TABLE 3. *Features of centrifugal and membrane plasma separation*

	Centrifugal method	Membrane method
I. Operational, system and module-related parameters	Whole blood and component flow rates Dimensions of centrifugal apparatus Angular velocity Radius of cell-plasma interface	Whole blood flow rate (shear rate) Plasma flow rate (filtration velocity) Transmembrane pressure Membrane structure (pore number and pore size) Filtration area Number of fluid paths Blood channel dimensions
II. Blood property effects	Cell diameter Cell concentration Specific weight of cell Specific weight of blood Viscosity of blood and plasma Sedimentation velocity of blood components	Cell properties Cell concentration Macromolecular concentration Viscosity of blood and plasma

ries for the treatment of both animals and humans. This instrument had a metal shield and different sized blades which folded out (Figs. 13 and 14).

For greater precision, the spring lancet was developed in the early 17th century. This instrument had a blade in a case connected to a coiled spring. When the spring recoiled, the blade was driven into the patient. This design alleviated the use of manual pressure.

Ambroise Paré, a young French army surgeon with troops of King François at Turin in 1536, had his first experience treating men for arquebus wounds. Running out of boiling oil (traditional treatment for gunshot injuries), he improvised, discovered that unburned patients healed much better, and resolved never to use hot oil again. It was some years later, in 1552, that Paré put aside cautery irons used to stop bleeding in amputations and reintroduced ligatures for tying blood vessels. During his life (1510–1590), Paré apprenticed as a barber–surgeon and became a master surgeon in 1536. Eventually Paré became known as the "Father of Surgery" (Fig. 15).

During the Middle Ages astrological influences played a part in the decision as to the best time to

TABLE 4. *Machines of centrifugal and membrane method*

Method of plasma separation	Equipment	
I. Intermittent centrifuge	Knightmage (manual)	Green Cross
	Haemonetics (manual)	Haemonetics Corp.
	30, 30-S	
	50, V50	
	PEX	
	Photopheresis (automated)	Therakos, Johnson & Johnson
II. Automated centrifuge continuous method	Celltrifuge	Fenwal Lab. (Amico)
	Celltrifuge II	
	CS-3000 Blood Cell Separator	Baxter
	IBM 2997 Blood Cell Separator	Cobe Lab. (IBM)
	Haemonetics	Haemonetics Corp.
	PCS, V50 Plus	
	Vivacell BT 798/CE	Dideco S.p.A.
III. Membrane method	Plasmapur, REDY 2000	Organon Teknika
	TPE System	Cobe
	BT 796	Dideco S.p.A.
	A 2008 PF	Fresenius
	Plasmapheresis Monitor	Organon
	Cryomax Model 360	Parker Medical
	Autophresis-C	Fenwal Lab.
	Plasauto 1000	Asahi Medical Co.
	Plasmapheresis Monitor KM-8500, 8800	Kuraray Co.
	KEM-21	Nikkiso Co.
	CP-1A	Terumo Co.
	KL-20, 30	Kawasumi
	Plasmat-secura	B. Braun

TABLE 5. *Centrifugal apheresis systems*

	Machine (manufacturer or selling agency)					
	Haemonetics PEX (Haemonetics Co.)	Celltrifuge (Fenwal Lab.)	CS-3000 Blood Cell Separator (Baxter)	IBM 2997 Blood Cell Separator (Cobe Lab.)	Vivacell BT 798/CE (Dideco S.p.A.)	UVAR Photopheresis Instrument (Therakos, J. & J. Co.)
Machine characteristics						
Power						
V	AC 220–240/110–220	AC 115	NA	AC 100	AC 110/220	NA
Hz, A	50/60, 4	50/60, 12	NA	NA	50/60	50/60, 12
Speed of centrifuge, rpm/g	0–4,800/NA	0–2,500/0–350	0–1,599/0–360	0–2,550 ± 150/NA	0–1,600/NA	0–4,800 ± 5%/NA
Weight, kg	84	158	315.2	263	235	107
Size (W × H × D), cm	35 × 132 × 76	122 × 95 × 80	60.9 × 144.2 × 97.8	101.6 × 78.7 × 73	64 × 133 × 95	41.9 × 88.9 × 63.5
Pump						
RBC pump	–	+	+	+	+	–
Plasma pump	–	+	+	+	+	–
WBC pump	–	+	+	+	+	+
Anticoagulant pump	+	+	+	+	+	+
Lubrication pump	–	+	–	+	–	–
Blood pump	+	–	–	–	+	+
Recirculation pump	–	–	–	–	–	–
Sensor (S)						
Pressure gauge	Occluded line +	Occluded line +	Return line + Access line + Blocked line +	Occluded line + Blocked line +	Access line +	Occluded line +
Air bubble detector	+	–	+	+	–	–
S of low level of fluid	–	Heparin +	+	+	+	–
S of overspeed or overheat of centrifuge	+	–	+	+	+	–
S of unbalanced centrifuge	–	–	+	–	+	–
S of humidity in the centrifuge	–	–	+	–	–	–
S of whole blood/anticoagulant	–	–	–	+	+	–
Detector of RBC	+	–	+	–	–	–
Photosystem	–	–	–	–	–	+
S of temperature in photoreceptor	–	–	–	–	–	+
Blood warmer (return line)	–	–	–	–	–	–
Operation	intermittent	continuous	continuous	continuous	continuous	intermittent
Blood flow, ml/min	50–80	40–150	35–80	40–70	40–70	30–50
Plasma separation speed, ml/min	25–35	25–35	25–35	20–35	20–35	*

NA, data not available from company; +, present; –, absent.

bleed a person suffering from a particular illness. Astrological charts like the one shown were printed depicting the influence of the stars and the signs of the zodiac on the various bodily parts (Figs. 16 and 17).

Cupping procedure

In 1888, the operation of cupping was performed by applying to the skin a glass or other form of cup after the air within it had been removed by heat or by suction (Fig. 18). In the dry method, the cup was applied to the unbroken skin, causing local subcutaneous trauma and acting as a counter-irritant. In the wet method the skin was scarified immediately before the cup was applied; this was a recognized method of bloodletting. Both methods probably had considerable psychological value as well. Cattle horns were among the first instruments used in the cupping process (Fig. 19). The Greeks and Romans preferred metal cups; glass cups date back to the 18th and 19th centuries.

For many years cupping and leeching were as closely related as eating and drinking. It is not surprising that the cupping machine invented by Demours was called an "artificial leech." Leeches are members of the Hirudinea division of the Chaetopod worms. Two varieties have been used in medicine: the horse leech and the species known as *Hirudo medicinalis.* These worms are fitted with chitinous jaws capable of producing a triangular or triradiate bit through which they can suck blood into their vast, expanding stomachs which fill the whole body. To prevent coagulation, an anticoagulant hirudin is injected into the wound, with the effect that when the leech is fully gorged and has fallen off, the blood

TABLE 6. *Therapeutic membrane apheresis systems*

	Autopheresis-C (Fenwal)	REDY 2000 (Organon Teknika)	TPE System (Cobe)	BT 796 (Dideco)	Cryomax Model 360 (Parker Biomedical)
Machine characteristics					
Power					
V	AC 115/230	AC 100/120	AC 125/250	NA	AC 100/120
Hz, A	47–65, NA	50/60, 6	50/60, 2/4.5	NA	60, 10
Weight, kg	47.7	62	61	NA	NA
Size (W × H × D), cm	43 × 67 × 26	89 × 127 × 56	56 × 147 × 25	NA	NA
Pump					
Blood pump	+	+	+	+	+
Plasma pump No. 1	+	+	+	+	+
Plasma pump No. 2	–	–	+	–	+
Recycle pump	–	–	–	–	–
Anticoagulant pump	+	+	+	+	–
Sensor					
Pressure gauge					
For access (arterial)	+	+	+	+	+
For return (venous)	+	+	+	+	+
For plasma	–	–	+	+	+
For TMP of 1st filter	–	–	–	–	+
For inlet of 2nd filter	–	–	–	–	+
Air bubble detector	NA	+	+	+	+
Detector of hemolysis	–	–	–	–	–
Display of total plasma flow	NA	–	+	–	+
Warmer of whole blood (B), plasma (P), and substitution (S)	NA	+, S	+, P	NA	+, B
Plasma cooler assembly	–	–	–	–	+

	Plasauto 1000 (Asahi Medical Co.)	Plasmapheresis Monitor KM-8500 (Kuraray Co.)	KEM-21 (Nikkiso Co.)	CP-1A (Termo Co.)	KL-30 (Kawasumi)
Machine characteristics					
Power					
V	AC 100/115 220	AC 100	AC 100	AC 100	AC 100
Hz-A	50/60, NA	50/60, NA	50/60, NA	50/60, NA	50/60, NA
Weight, kg	50	60	70	66	40
Size (W × H × D), cm	60 × 142 × 56	43 × 130 × 41	48 × 141 × 50	51 × 66 × 36	34 × 38 × 54
Pump					
Blood pump	+	+	+	+	
Plasma pump No. 1	+	+	+	+	+
Plasma pump No. 2	+	+	+	+	+
Recycle pump	+	+	+	+	–
Anticoagulant pump	+	+	+	+	+
Sensor					
Pressure gauge					
For access (arterial)	+	+	+	+	+
For return (venous)	+	+	+	+	+
For plasma	+	–	+	+	+
For TMP of 1st filter	+	+	+	+	+
For inlet of 2nd filter	+	+	–	+	+
Air bubble detector	+	+	+	+	+
Detector of hemolysis	–	–	D. of RBC	–	+
Display of total plasma flow	+	+	+	+	+
Warmer of whole blood (B), plasma (P), and substitution (S)	+, B	+, P	+, NA	+, NA	+, B
Plasma cooler assembly	–	–	–	–	–

NA, data not available from company; +, present; –, absent.

TABLE 7. *Physical characteristics of membrane filters in plasmapheresis*

Supplier or manufacturer	Filters	Membrane material: hollow fiber (F) or plate or pile (P)	Surface area (m^2)	Maximum pore size (μm)
Plasma separator				
Travenol Lab., USA	CPS-10	Polypropylene (F)	0.17	0.55
AB Gambro, USA	Fiber plasmafilter PP	Polypropylene (F)	0.38	0.5
	Fiber plasmafilter PC-1000	Polycarbonate (F)	0.27	NA
Cobe Lab, USA	TPE plasma separator	Polyvinylchloride (P)	0.13	0.6
Fresenius MTS, FRG	Plasmaflux P2	Polypropylene (F)	0.50	0.5
Dideco S.p.A., Italy	Hemaplex BT 900	Polypropylene (F)	0.20	0.5
Asahi Medical, Japan	Plasmaflo AP-06-M	Cellulose diacetate (F)	0.65	0.2
	Plasmaflo AP-03-H	Cellulose diacetate (F)	0.30	0.2
	Plasmaflo AP-05-H	Cellulose diacetate (F)	0.50	0.2
	Plasmaflo AP-08-H	Cellulose diacetate (F)	0.80	0.2
Kuraray Co., Japan	Plasmacure type 'M'	Polyvinylalcohol (F)	0.30	0.2
(Kawasumi Lab. Inc.)	Plasmacure type 'L'	Polyvinylalcohol (F)	0.50	0.2
Toray Ind., Japan	Plasmax PS-05	Polymethylmethacrylate (F)	0.50	0.5
	Plasmax PS-02	Polymethylmethacrylate (F)	0.15	NA
Teijin, Japan	Plasma separator TP 50	Polymer alloy (F)	0.40	0.2
Mitsubishi, Japan	Plasma separator MPS 0250	Polyethylene (F)	0.50	NA
Terumo, Japan	PS-4000	Cellulose acetate (P)	0.50	0.45
Organon Teknika, USA	Curesis	Polypropylene (F)	0.12	0.65
Cordis Dow Inc.	Plasmafilter	Polyethylene (F)	0.70	NA
Nipro, Japan	Plasma separator PEX-50	Cellulose triacetate (F)	0.50	0.4
Kawasumi Lab. Inc.,	Plasma separator KPS02	Polypropylene (F)	0.20	0.6
Japan	Plasma separator KPS03	Polypropylene (F)	0.30	0.6
	Plasma separator KPS04	Polypropylene (F)	0.40	0.6
Plasma fractionator				
Dideco, S.p.A., Italy	Albusave BT 902	Cellulose diacetate (F)	1.00	0.02
Enka AG	PF prototype	Cellulose acetate (F)	1.00	NA
Ashai Medical, Japan	Cascadeflo AC-1730	Cellulose diacetate (F)	1.70	NA
	Cascadeflo AC-1760	Cellulose diacetate (F)	1.70	NA
	Cascadeflo AC-1770	Cellulose diacetate (F)	1.70	NA
	Plasmaflo AP-06-M	Cellulose diacetate (C)	0.65	0.2
Kuraray Co., Japan	Eval filter type '2A'	Ethylene vinyl alcohol (F)	1.00	0.01
	Eval filter type '3A'	Ethylene vinyl alcohol (F)	NA	0.02
	Eval filter type '4A'	Ethylene vinyl alcohol (F, T)	2.00	0.03
Toray Ind., Japan	Plasmax AS-08	Polymethylmethacrylate (F)	0.80	NA
	Plasmax ASC-08	Polymethylmethacrylate (F)	0.80	NA
Teijin, Japan	TA-100	Cellulose diacetate (F)	0.80	NA
	TA-200	Cellulose diacetate (F)	0.80	NA
Terumo, Japan	CF-01	Cellulose acetate (F)	1.00	NA

EOG, ethylene oxide gas; SAC, stream autoclave; γ, gamma rays; NA, data not available from company.

continues to flow freely. Botallus, living in the 16th century, was one of the warmest partisans of frequent bleeding and found leeches most useful if applied to the small parts of the body, the ears, nostrils, and fingers in particular (Fig. 20).

Scarificators were invented between 1708–1719 and were used to sever capillaries prior to the cupping procedure (Fig. 21). The earliest scarificators consisted of a square brass box with cocking and release levers and sixteen pointed blades. The instrument had a screw which allowed for the adjustment of the blade depth (Fig. 22).

BLOOD TRANSFUSION

Only in the last century has the lifesaving potential of blood and its components been truly appreciated. Now the use of blood transfusion ranks as one of the foremost therapeutic advances for the restoration of health, involving the use of whole blood, its separated components, its plasma and plasma derivatives.

The beginnings of transfusion therapy date from the mid-17th century following Harvey's momentous discovery of the circulation of blood, which first stimulated research on animals and then on man. By 1665, Lower, in England, performed and described the first animal transfusions, whereas Denis, in France, is credited with the first successful transfusions in humans (Fig. 23).

The importance of blood in carrying oxygen from the lungs to the tissues of the body was not appreciated until the experiences of Priestly in 1774 and Lavoisier in 1777 on oxygen and its role in respiration. The danger of acute blood loss could then be interpreted and known, making transfusion a logical

TABLE 7. *Continued*

Inner fiber or plate spacing (μm)	Priming volume (ml;inner/outer)	Number of fibers or plates	Length (cm; full/exposed)	Sterilization
320	17/178	800	26.0/21.4	EOG
330	36/88	2,000	21.0/17.0	NA
270	24/NA	2,000	21.0/17.0	NA
NA	18/NA	6	22.0/16.0	EOG
330	48/290	2,250	25.0/20.0	EOG
320	18/NA	900	25.4/21.0	NA
370	95/NA	3,100	28.3/18.3	EOG
330	45/NA	NA	NA/13.0	EOG
330	65/NA	3,000	26.5/15.7	EOG
330	90/NA	NA	NA/18.3	EOG
300	40/NA	1,750	18/16	SAC
300	60/NA	1,850	23.4/20	SAC
370	59/102	2,500	22.0/17.5	γ
370	19/NA	950	18.0/13.5	γ
320	32/NA	1,600	NA/25.0	EOG
270	45/NA	3,640	21.5/16.5	EOG
80	80/120	30	45	EOG
330	12/NA	800	25.0/NA	NA
270	66/NA	5,500	21.0/16.0	NA
285	NA/NA	NA	NA	EOG
330	23/NA	NA	NA	SAC
330	34/NA	NA	NA	SAC
330	46/NA	NA	NA	SAC
350	170/NA	NA	NA/23.5	EOG
440	121/NA	3,000	26.5/21.5	NA
220	130/NA	NA	28.3/18.3	EOG
220	130/NA	NA	28.3/18.3	EOG
220	130/NA	NA	28.3/18.3	EOG
370	95/NA	3,100	28.3/18.3	EOG
200	100 (1 m^2)	8,000 (1 m^2)	23/19.0 (1 m^2)	EOG
200	NA	NA	NA	EOG
200	130 (2 m^2)	11,000 (2 m^2)	27/23.0 (2 m^2)	EOG
370	97/156	3,950	23.0/19.5	γ
370	97/156	3,950	23.0/19.5	γ
250	50/NA	NA	NA/25.0	NA
250	50/NA	NA	NA/25.0	NA
NA	NA/NA	NA	NA/70	EOG

mode of therapy. The discovery of the human blood groups (ABO) by Landsteiner in 1901 was one of the most important advances toward safe and effective transfusions. The significance of isoagglutinins and their relation to transfusion reactions, hemolysis, and the typing and cross matching of donors, were of fundamental importance to the practice of transfusion and in the future to the pathogenesis of a number of diseases.

The development of anticoagulants took blood transfusion out of the hands of the surgeons. Overcoming the problems of blood clotting led to the development of transfusion therapies, to the storage of blood, eventually to the beginning of blood banks, to the separation of blood elements and their specific uses, and finally to the fractionation and concentration of plasma components.

The first operating hospital blood bank in the United States was organized by Fantes in 1937 at the Cook County Hospital in Chicago, Illinois. Blood was preserved with 2% sodium citrate and used within 7–10 days. The need for blood became more acute in World War II, and blood procurement organizations quickly expanded, especially in Great Britain. By 1947, the American National Red Cross formulated a plan for the establishment of regional blood centers to supply blood and blood products. Hospital blood and community blood banks formed an organization called the American Association of Blood Banks in 1948.

Originally all blood was collected in rubber stoppered bottles with rubber connecting tubes and steel needles, all of which were reused after being washed and resterilized. A high incidence of pyrogen reactions was reported and soon disposable tubing replaced the rubber connecting tubes for the donor and the recipient's sets. Plastic collection bags for blood had been developed by 1949.

TABLE 8. *Affinity-type sorbents*

Ligand or material of adsorption	Agent sorbed
Polylysin methylated albumin	T4 phage DNA
Anion-exchange resin	bilirubin[a]
Polyanion	
Dextran sulfate	LDL[a]
Heparin:heparin agarose	LDL
Tryptophan IM-TR	anti-acetylcholine receptor Ab[a], IC, RF[a]
Phenylalanine IM-PH	anti-MBP Ab[a], IC, RF
Modified PVA gel I-02	RF, IC, anti-DNA Ab anti-RNP ab anti-SM Ab
Oligosaccharide	anti-blood type AB
Charcoal sorbent	bilirubin, creatinine urea, potassium
DNA	anti-DNA Ab[a]
Ag Blood-type Ag	anti-blood type Ab[a]
Insulin	anti-insulin Ab
Factor VIII	anti-factor VIII Ab[a]
Factor IX	anti-factor FIX ab
Anti-LDL Ab	LDL[a]
Ab Anti-α Feto ab	α-Fetoprotein
Anti-HBS Ab	HBS
Anti-IgE Ab	IgE
Clq	IC
Protein A	Ic, IgG[a], Cl

[a] Clinical application stage.
PVA, polyvinyl alcohol; RF, rheumatoid factor; IC, immune complexes.

In 1943, Loutit and Mollison developed an acid–citrate–dextrose (ACD) solution, and this remained the standard for the 21-day preservation of blood. The introduction of citrate–phosphate–dextrose (CPD) solution by Gibson in 1957 extended the storage period to 28 days with a loss of less than 30% of the red cells. Within the next decade, all blood banks

FIG. 4. This early 14th century (A.D. 1315) Syrian painting depicts two Arab scribes sitting on top of a bloodletting device counting each drop of blood as it falls to the basin below. The script on the right says they must alternatively count three gram units of blood, called dirhans, until approximately twenty ounces of blood has been drained. Pulleys are attached to the scribes' arms and more their pens as the basin fills with blood (from the Freer Gallery of Art, Smithsonian Institution, Washington, D.C., with permission).

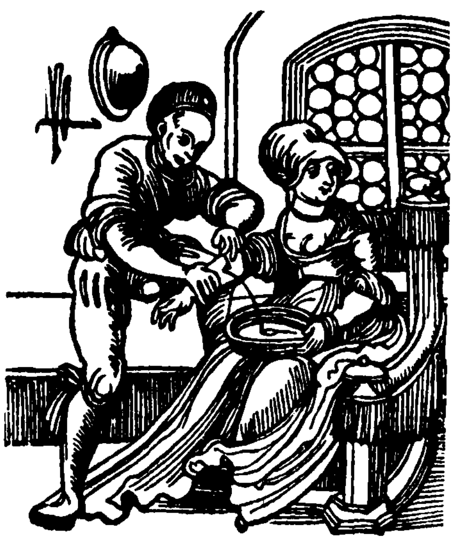


FIG. 3. Phlebotomy, 1520 (from the National Library of Medicine, Bethesda, Maryland).

FIG. 5. Hippocrates: medicine becomes a science (from Parke-Davis, Division of Warner-Lambert Co., with permission).

FIG. 6. Galen, influence for forty-five generations (from Parke-Davis, Division of Warner-Lambert Co., with permission).

converted to the use of CPD solutions although the dating period by government regulations remained at 21 days.

Forty years ago, blood banks served to supply only two items, specifically whole blood and plasma from outdated blood. Today, any hospital can have available many preparations including:

- Whole blood in ACD or CPD, 2–21 days old, of group and type specific varieties
- Heparinized whole blood
- Packed red cell concentrates

FIG. 7. Achilles bandaging the arm of Patrokles. From a plaque Sofias dated about 500 B.C. (from Parke-Davis, Division of Warner-Lambert Co., with permission).

FIG. 8. Bloodletting as depicted by Peytel. Below the patient is an ancient bleeding bowl (from Musée du Louvre, Paris, with permission).

FIG. 9. Body fluids of antiquity, called humors, served as medieval notions for health and disposition. We still speak of good and bad humors to describe temperament and mood. Melancholy is synonymous with sadness and phlegm with unemotional reactions. Sanguine refers to a ruddy or cheerful person, while choleric describes an irritable one (from Zentralbibliotehek, Zurich, with permission).

- Washed red blood cell concentrates free of plasma, platelets, or white cells for highly sensitized recipients
- Red cell packs irradiated for immunodeficient patients
- Platelet concentrates procured by thrombopheresis
- White cell concentrates prepared by leukopheresis
- Plasma, fresh or stored
- Albumin
- Cryoprecipitates
- Factor VIII
- Factor IX concentrate for hemophilia patients
- Fibrinogen
- Gamma globulin derivatives from normal plasma
- Anti-RH gamma globulin from sensitized RH negative donors
- Gamma globulin from high antibody level serum

William Harvey's discovered of the circulation of the blood was momentous as a step toward transfusion therapy. In his treatise, *De Motu Cordis,* Harvey described how the blood circulated within the body in a closed system. He thought of the heart as a pump which sent blood to the arms and legs through arteries and back to the heart through the veins (Figs. 24–26).

Oscar Hasse (1837–1898) advocated the use of sheep's blood for transfusion of various incurable diseases. In 1874, he reported fifteen such transfusions which he had performed (Fig. 27). The drawing is an artist's version of Hasse's method with the woman being transfused lamb's blood. Also shown (Fig. 28) are replicas of the silver cannulae Hasse used for direct transfusion of the lamb's blood.

Dr. J.H. Aveling was an exponent of the direct or immediate method of transfusion of blood. In 1863, he invented the simple apparatus shown which consisted of an India-rubber tube with a small rubber bulb in the middle which acted as an auxiliary heart. There were two silver tubes to enter the veins and two stopcocks. With this apparatus changes of coagulation were minimized (Fig. 29).

FIG. 10. Barber pole, circa 1905 (from Carson Barber Supplies, Cleveland, with permission).

George W. Crile (1864–1943)

Dr. Crile was one of the first to use blood transfusion therapeutically. He devised the technique of direct suturing of the recipient. In August 1906, at St. Alexis Hospital in Cleveland, George Crile performed the first successful direct blood transfusion on a human being (Figs. 30–33).

Born in Chile, Ohio, in 1864, he attended Northwestern Ohio Normal School and received his medical training at the University of Wooster in Cleveland in 1887.

FIG. 11. Clockwise from the top: porringer, barber's basin, bleeding bowl (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

Together with Frank E. Bunts, William E. Lower, and John Phillips, Crile founded the Cleveland Clinic in 1921. Today the Cleveland Clinic Foundation maintains an international reputation as a leader in innovative medicine and research.

Following the Carrel technique, Crile used the silver cannula he developed to join the severed ends of the recipient's and donor's blood vessels through anastomosis: (a) the recipient's vein was pulled through the cannula; (b) the vein was cuffed and tied into place in the groove near the handle of the cannula; (c) the donor's artery and the recipient's vein were connected (Figs. 34–39).

FIG. 12. In *Don Quixote de la Mancha,* Miguel de Cervantes Saavedra used this type of bowl as the "Helmet of Mambrino" (from the Historical Collection of Electro-Medical and Quack Devices of O. Lindan, Cleveland, Ohio).

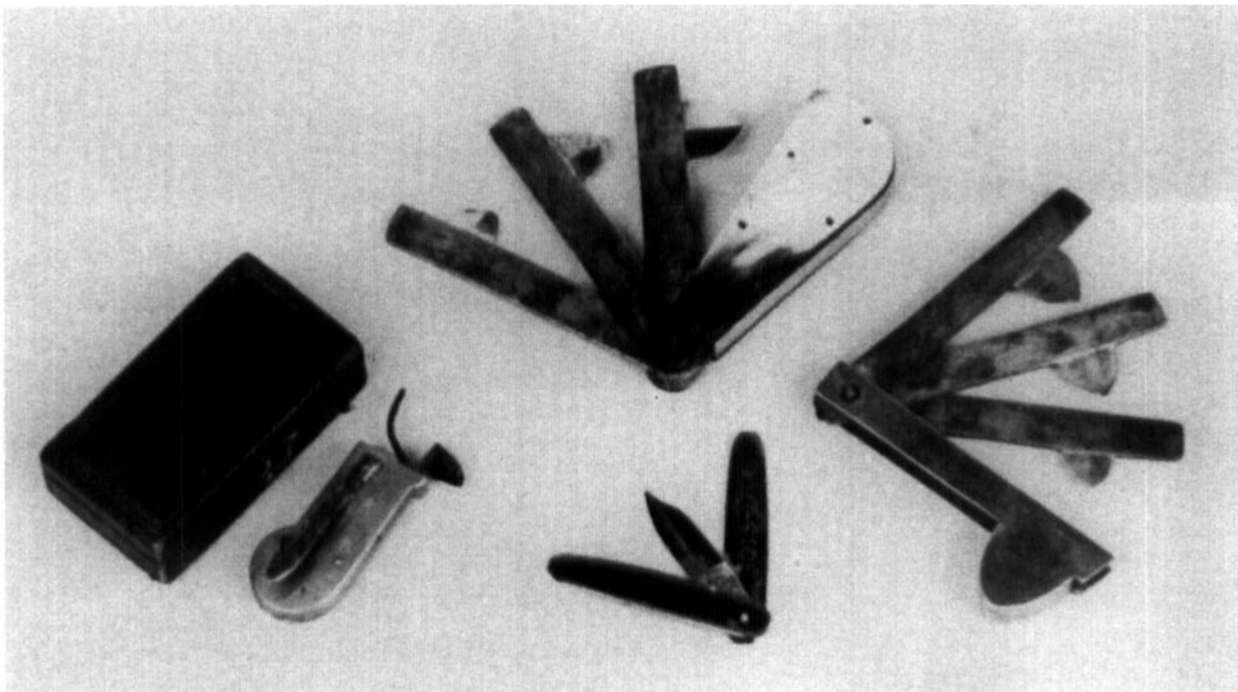


FIG. 13. Bloodletting instruments clockwise from the top: fleam with horn shield, fleam with brass shield, thumb lancet, spring lancet with box (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

BLOOD PURIFICATION, FOLK MEDICINE, AND QUACKERY

Throughout the history of man, there has been an intuitive belief that impurities or poisons in the body cause disease (11). The ancient procedures for body cleaning, such as purging, use of emetics, enemas, inducing perspiration, diuresis, and bloodletting persisted as the most important therapeutic procedures and were used indiscriminately for 3,000 years in Western civilization. They ceased to be fashionable about 100 years ago, although they can still be found today in Folk Medicine and in so-called unorthodox healing (Figs. 40–46).

Bloodletting was considered a panacea for most ailments throughout its history from Egyptian times to the middle of the last century although there were occasional dissenters to its unrestrained use. When it was applied, it was on a purely empirical and not a scientific basis. Thus, it represented medicine as an art and not a rational procedure. Among various beliefs for the use of bloodletting, there was one which, although not much stressed at the time, is of interest to us. It was popularly believed that the unhealthy as well as the old blood has to be periodically removed not only from the sick but even from healthy people. It was supposed to stimulate the production of young fresh blood and thus restore the vigor of life.

It is fascinating to reflect that this old intuitive believe in the necessity of periodically purifying the blood is now implemented scientifically by the processes of hemodialysis, blood exchanges, and plasmapheresis.

History teaches us that any new or rediscovered medical concept, when enthusiastically accepted, carries with it a danger of indiscriminate use. Only with time does a balanced evaluation become possible (10).

Wittke's Health Restorer (1915) was manufactured in Mayville, Wisconsin, and was advertised as "one of the most successful treatments for illness that the world has ever known." The instrument consisted of a polarizer, cords, and treating discs which were nickel plated. Within the polarizer was a quantity of mineral metallic substances. The original cost of the health restorer was $35 (Fig. 47).

The Penny Arcade Electric machine manufactured by the Advance Machine Company, Chicago, Illinois, in 1916, provided the opportunity to increase the circulation and purify the blood for one penny (Fig. 48).

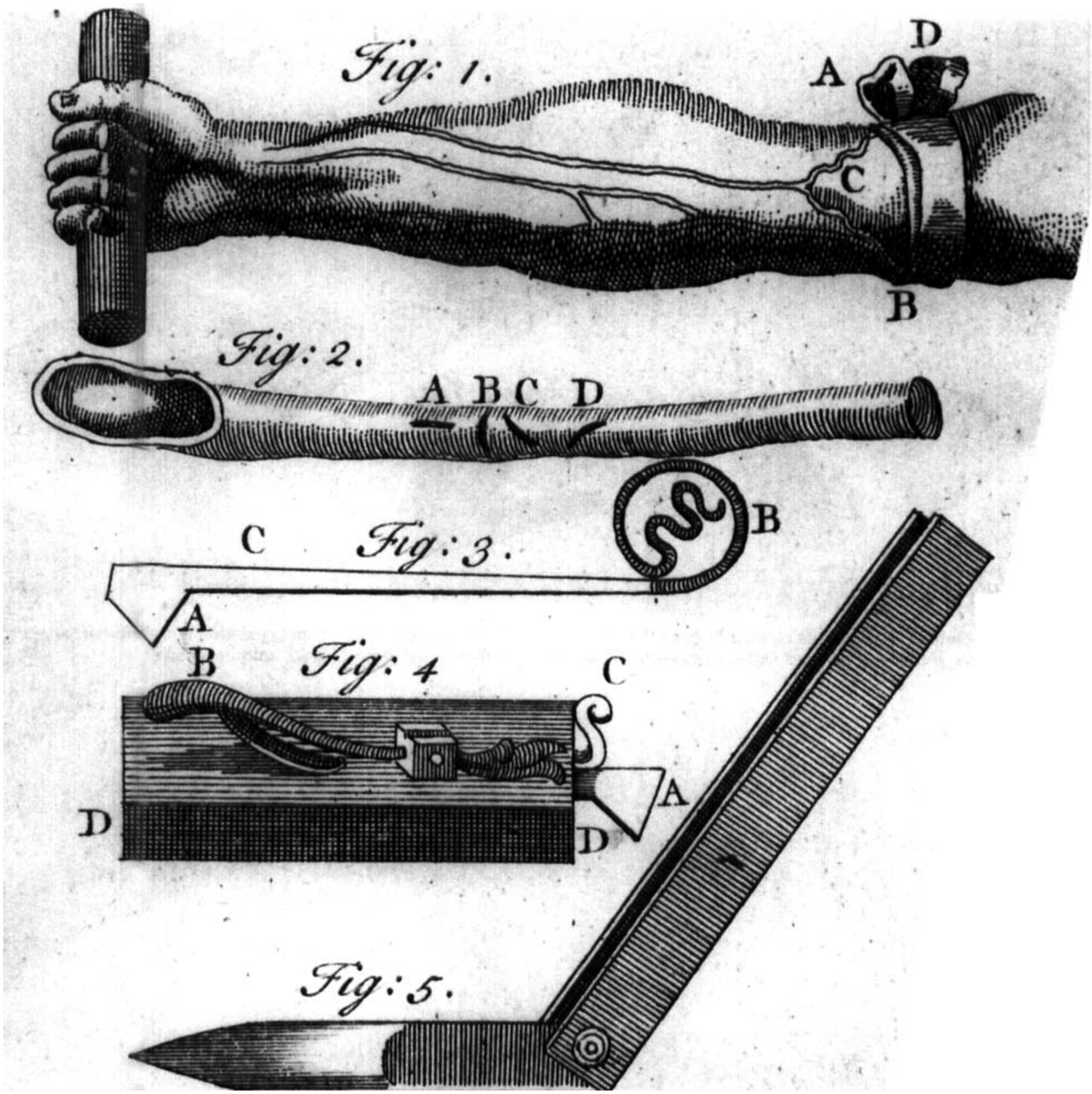


FIG. 14. Shown are instruments and techniques of bloodletting in the mid-eighteenth century. Figure 1 illustrates the common veins bled, Fig. 2 the various types of incisions, Fig. 3 a fleam, Fig. 4 a spring lancet, and Fig. 5 is an example of a "French lancet" (from the National Library of Medicine, Bethesda, Maryland, with permission).

Richardson's magneto-galvanic "medallion" (circa 1870–1885) was manufactured by A.M. Richardson and Company, New York City (Figs. 49–50). It was billed as an alternative to drugs and was thought to cure a variety of illnesses. "It will infuse 'electricity' into your system, invigorating, stimulating, and putting new life in every nerve in your body."

FIG. 15. Ambroise Paré: surgery acquires stature (from Parke-Davis, Division of Warner-Lambert Co., with permission).

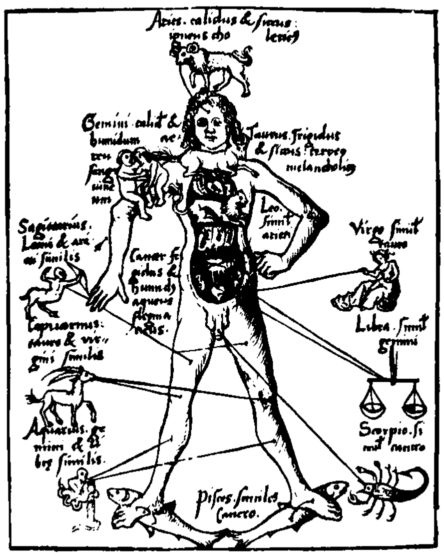


FIG. 16. Zodiacal man, circa 1300 (from Ann Ronan Picture Library, Cambridge, England, with permission).

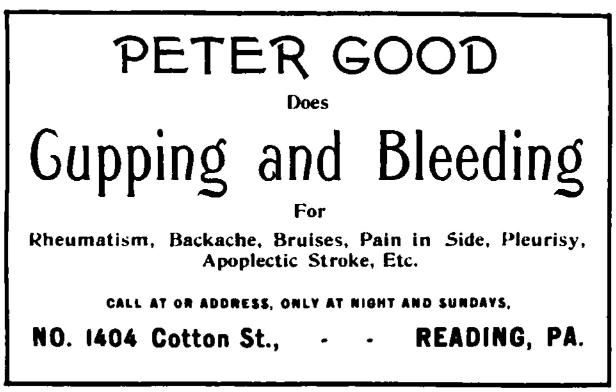


FIG. 17. Barber–surgeon's calling card, circa 1860 (from the National Museum of American History, Washington, D.C., with permission.)

FIG. 18. Early cupping set which includes several vessels of various sizes and an alcohol lamp (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

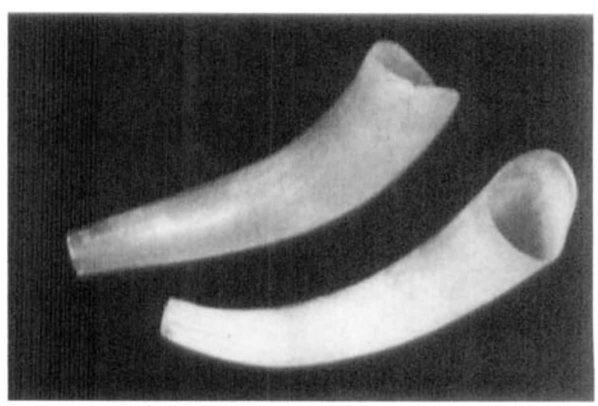


FIG. 19. Cattle horns (from H. Kambic).

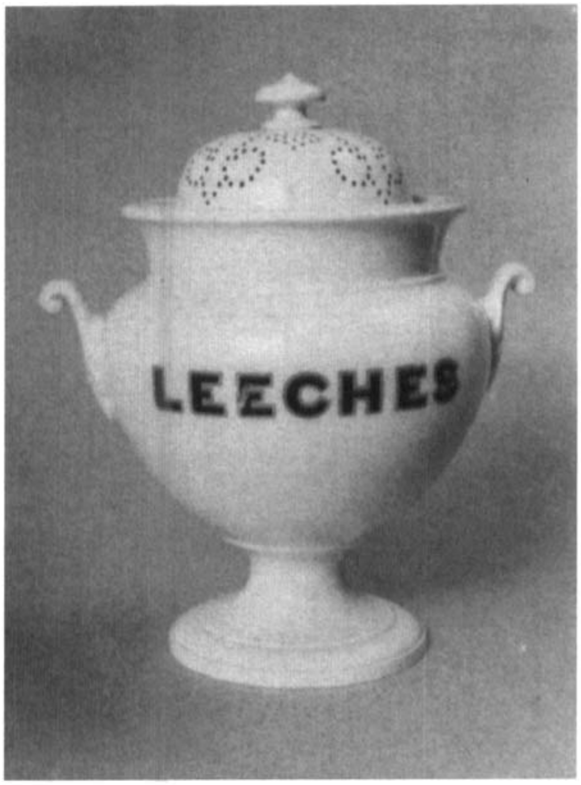


FIG. 20. Leech jar (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

FIG. 21. Scarification scene, 1719. In order to obtain sufficient blood, 20 to 40 slashes were made in the patient's legs, and the patient then stood in a basin of warm water (National Library of Medicine, Bethesda, Maryland, with permission).

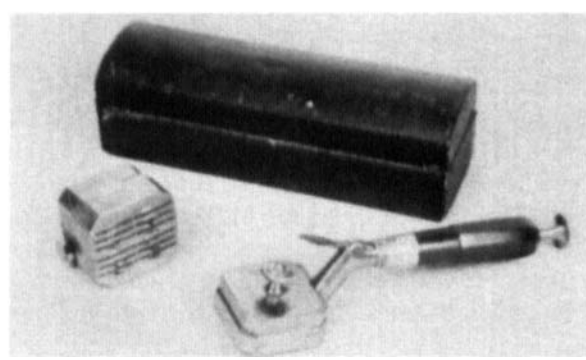


FIG. 22. Blade scarificator; patent model of Tiemann's scarificator, with box.

FIG. 23. Animal blood was used in transfusions of humans until the early 19th century. The early transfusions were most commonly attempted in an effort to cure insanity or long-lasting unremitting disease. This illustration depicts a blood transfusion in the 17th century. After an etching by Johannis Scultiti (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

"From the date of this first successful case of blood transfusion by an end-to-end suturing of the vessels of one human being to another, it was nearly thirty years before transfusion was accepted except by medical men of high standing. Yet I had demonstrated its importance in hemorrhage and shock; had used it clinically since 1905; had published a monograph on *Hemorrhage and Transfusion* in 1909 and for ten years colleagues and students from various centers had witnessed its value at our clinic, but not until after the First World War was it used generally as a method of counteracting all forms of hemorrhage as well as depleted states. Such is the inertia of the human race."

—George W. Crile

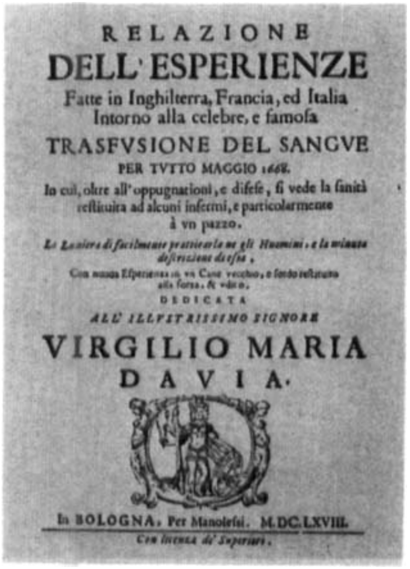

RELAZIONE
DELL' ESPERIENZE
Fatte in Inghilterra, Francia, ed Italia
Intorno alla celebre, e famosa
TRASFVSIONE DEL SANGVE
PER TVTTO MAGGIO 1668.
In cui, oltre all'oppugnationi, e difese, si vede la sanità restituita ad alcuni infermi, e particolarmente à vn pazzo.
DEDICATA
ALL' ILLVSTRISSIMO SIGNORE
VIRGILIO MARIA
DAVIA.
In BOLOGNA. Per Manolessi. M.DC.LXVIII.

FIG. 24. Title page of the first textbook on blood transfusion printed in 1668 (from *Blood Transfusion,* G. Keynes, Williams & Wilkins, Baltimore, Maryland, with permission).

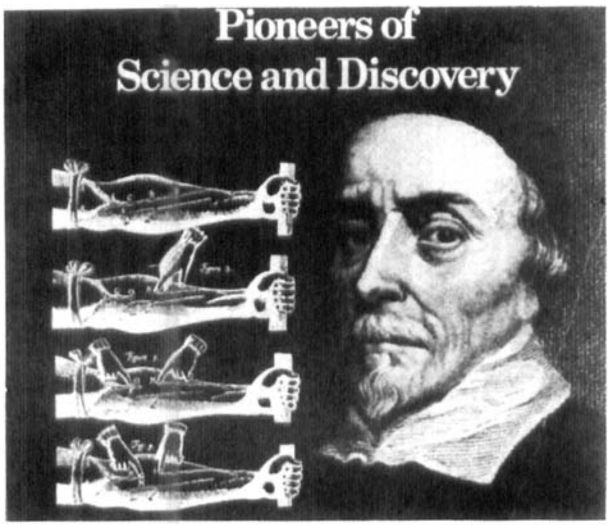


FIG. 25. William Harvey, 1568–1637 (from *Pioneers of Science and Surgery: William Harvey and the Circulation of Blood,* Wayland, East Sussex, with permission).

FIG. 27. Sheep blood transfusion (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

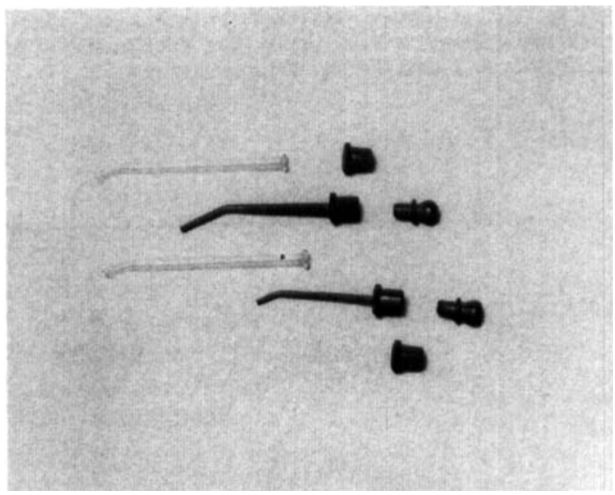
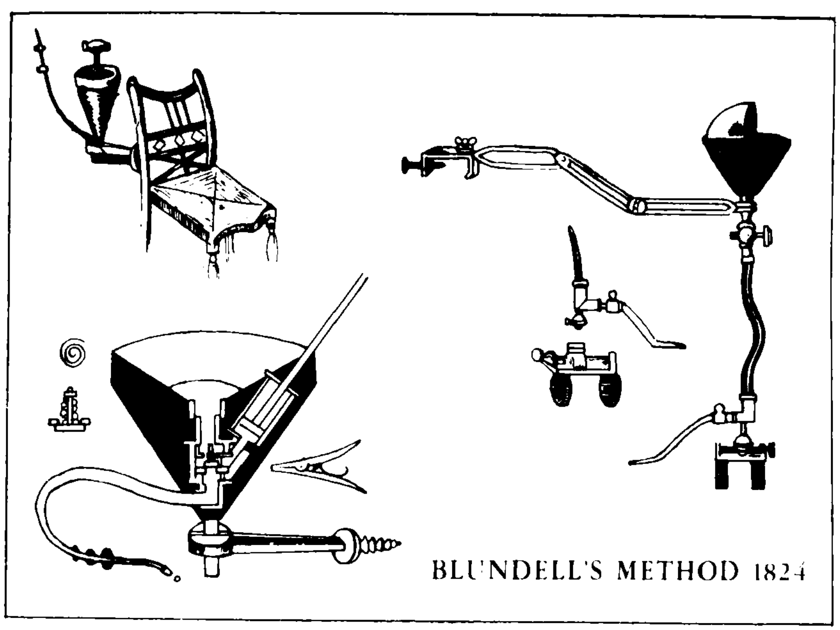


FIG. 28. Silver cannulae used by Hasse (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

FIG. 26. James Blundell devised several instruments for his transfusion method. Upper left: the "impellor" was attached to a chair where the donor sat. Lower left: cross section of the "impellor" which shows a syringe and valve mechanism for changing the direction of the blood flow. Right: view of the whole apparatus (from *The Blood Bank and the Technique and Therapeutics of Transfusion,* Kilduff, R.A. and M. DeBakey, C.V. Mosby Co., with permission).



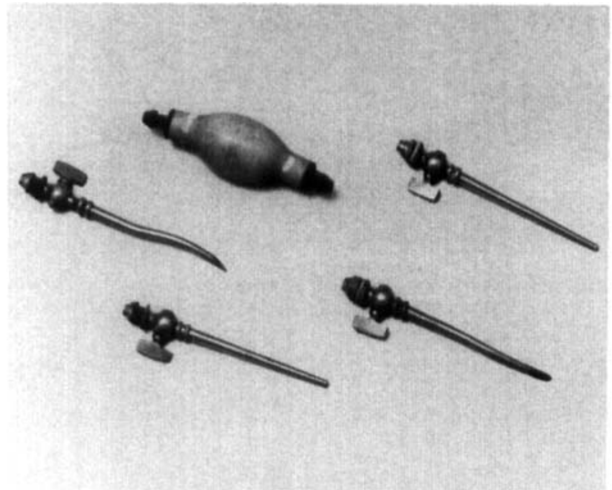


FIG. 29. Aveling transfusion apparatus (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

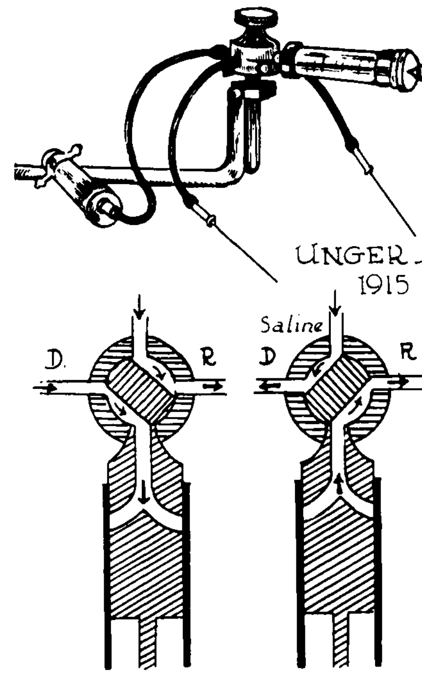


FIG. 31. Unger's instrument used the principle of a two-way stopcock. This feature allowed for blood to be drawn through a needle in the donor's vein. Once the stopcock was turned, the recipient could be injected with the donor's blood (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

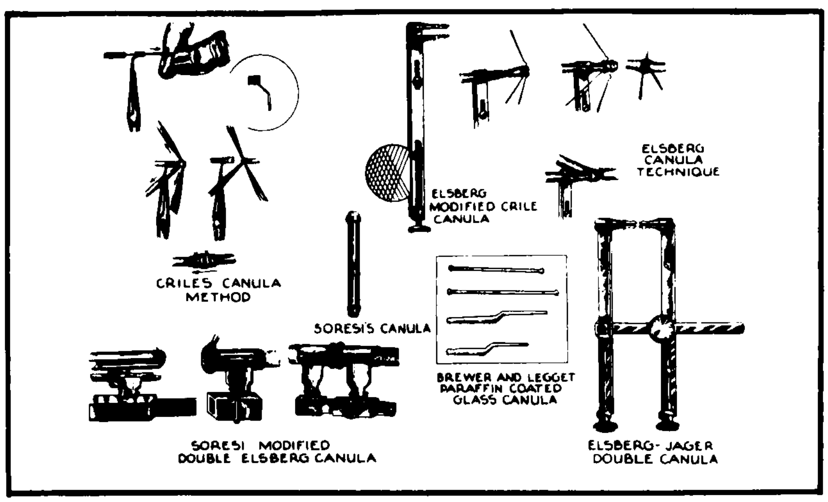


FIG. 30. Drawings of the progressive development of cannulae used in blood transfusions (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

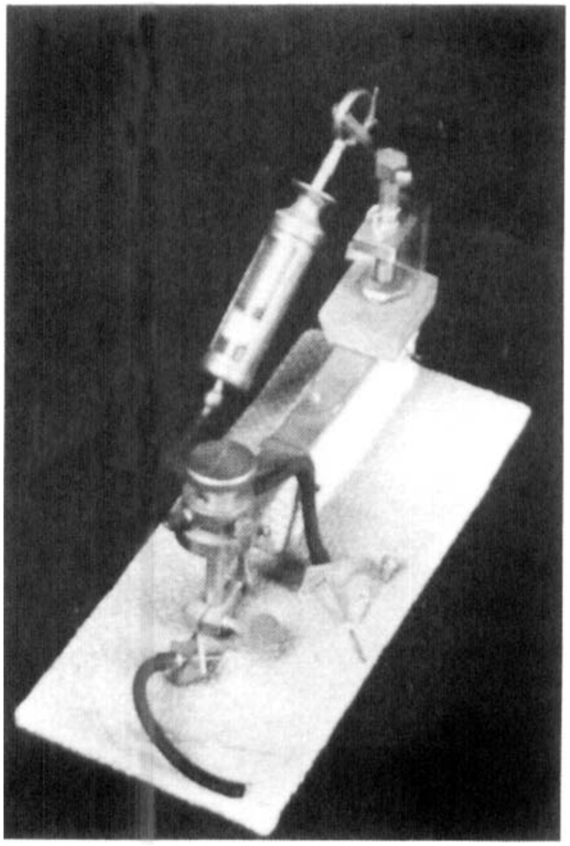


FIG. 32. Unger's instrument for syringe transfusion included the following: (a) stopcock; (b) blood syringe connected to the blood outlet; (c) saline syringe connected to saline outlet; (d) donor's cannula connected to the donor's outlet; and (e) the recipient's cannula connected to the recipient's outlet (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

FIG. 33. George W. Crile (from the Archives at the Cleveland Clinic Foundation, Cleveland, Ohio, with permission).

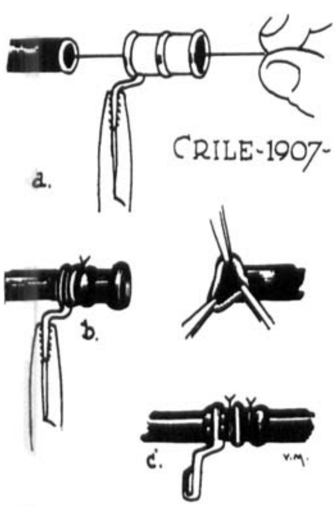


FIG. 34. The method perfected by Crile had the advantage of preventing blood leakage during the process and it allowed for an uninterrupted flow of blood without clotting (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

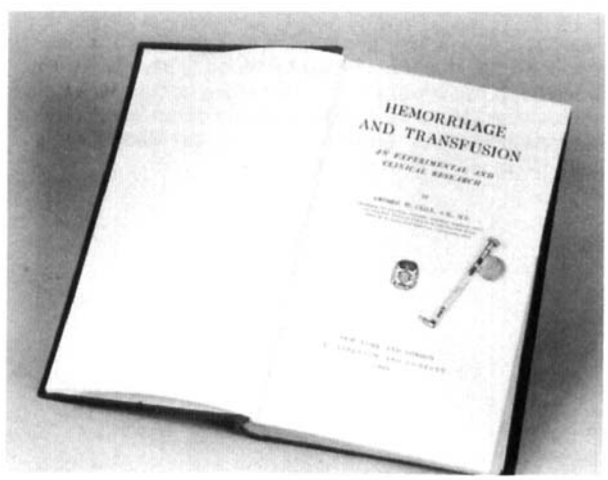


FIG. 35. The title page of the book *Hemorrhage and Transfusion* written by Crile and published in 1909. A modification of Crile's original cannula by Elsberg in 1909 is placed on the book (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

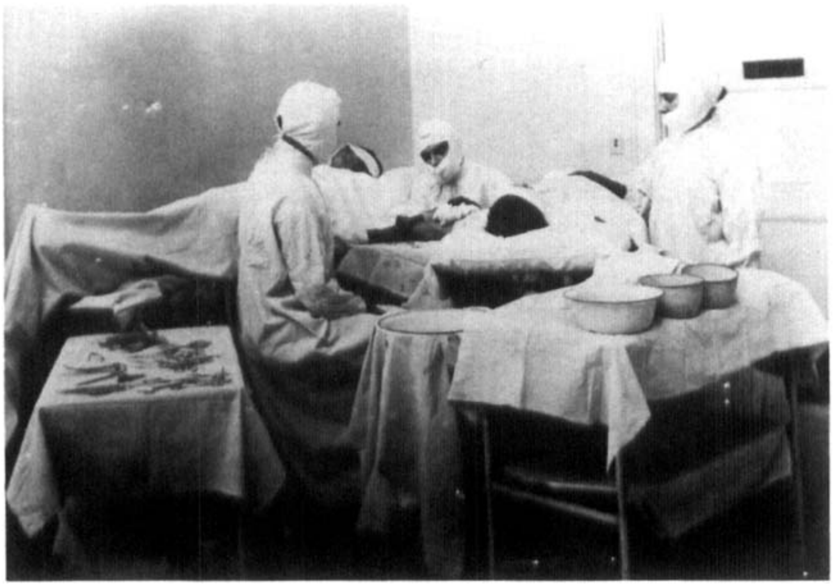


FIG. 36. The first successful case of blood transfusion between one human and another took place in St. Alexis Hospital in Cleveland, Ohio, in 1906, and was performed by Dr. George Crile using the technique of end-to-end anastomosis developed by Carrel (from the Cleveland Clinic Foundation Archives, with permission).

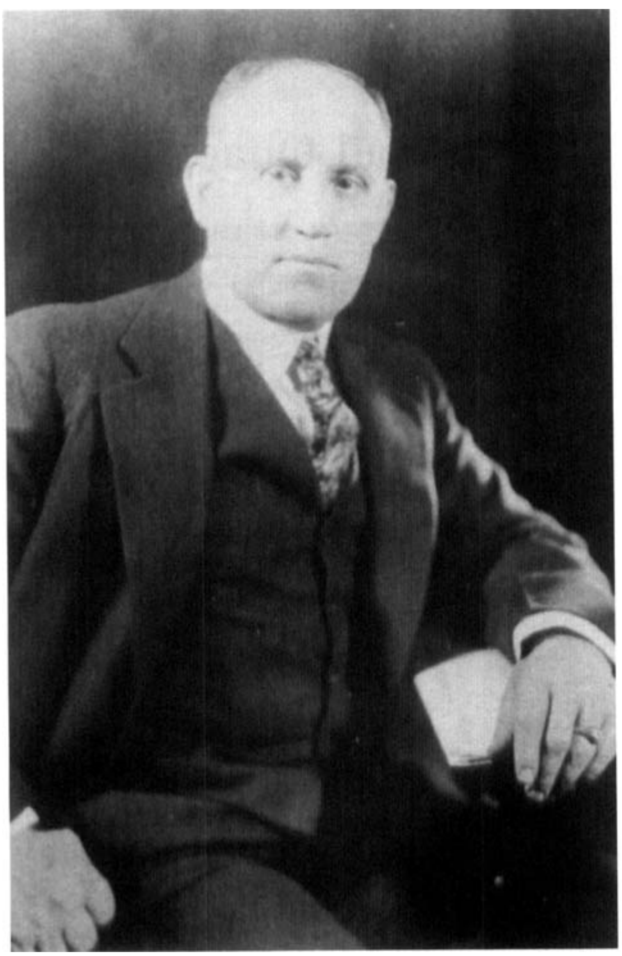


FIG. 37. J.H. Miller was the recipient of George Crile's first successful blood transfusion at St. Alexis Hospital. Miller, a Russian, was twenty-three at the time. Following nephrectomy upon an enlarged kidney, he suffered a secondary hemorrhage. The blood transfusion was the last desperate attempt to keep the dying patient alive (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

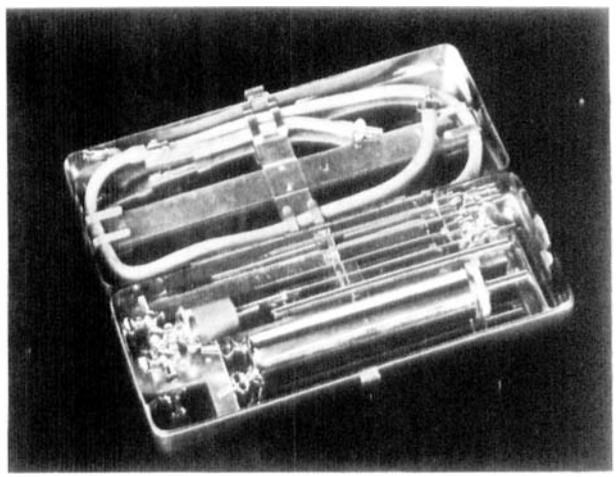


FIG. 38. Transfusion set used in the 1930s (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

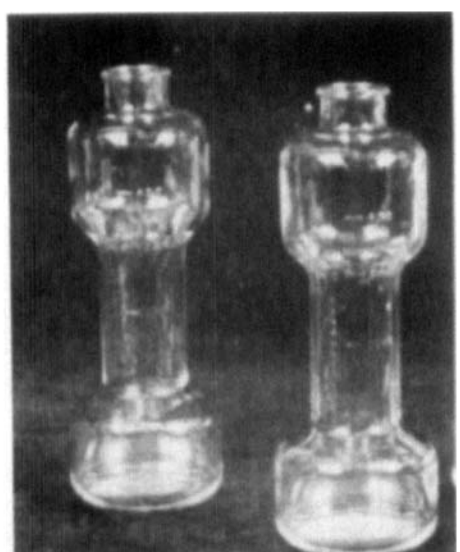


FIG. 39. Blood transfusion bottles used prior to 1965 for the separation of plasma (from the Dittrick Medical History Center of the Cleveland Health Sciences Library, Cleveland, Ohio, with permission).

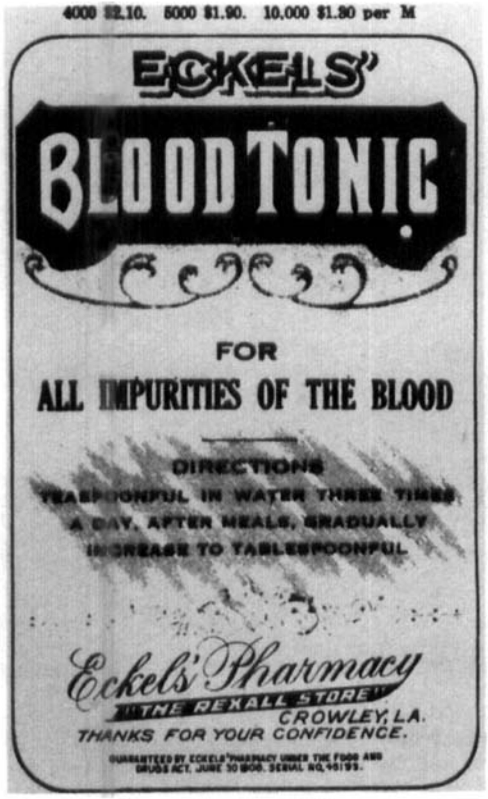


FIG. 40. Folk medicine advertisement (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

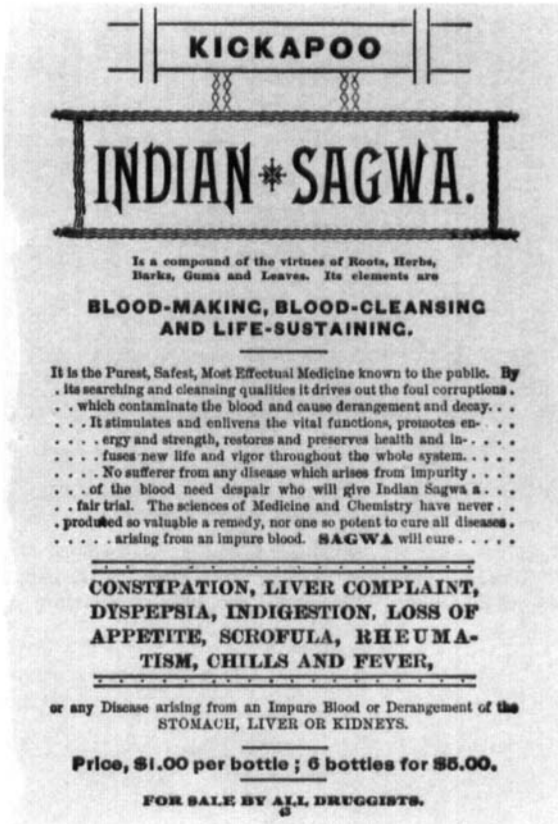


FIG. 42. Folk medicine advertisement (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

THE POETRY OF PILLS

"To purify the stagnate blood,
Restore the flush of health,
A medicine to do this good
Is worth a monarch's wealth;—
Though chills and fever make you feel
As limber as a rag,
You'll soon become as smart as steel,
By the pills of Doctor Bragg."

The *Iowa Standard* of Iowa City, August 18, 1847

FIG. 43. From the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission.

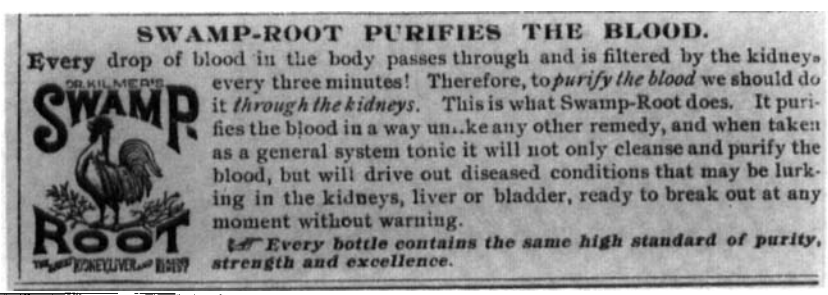


FIG. 41. Folk medicine advertisement (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

FIG. 44. From the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission.

FIG. 45. Another advertisement for a "blood purifier" (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

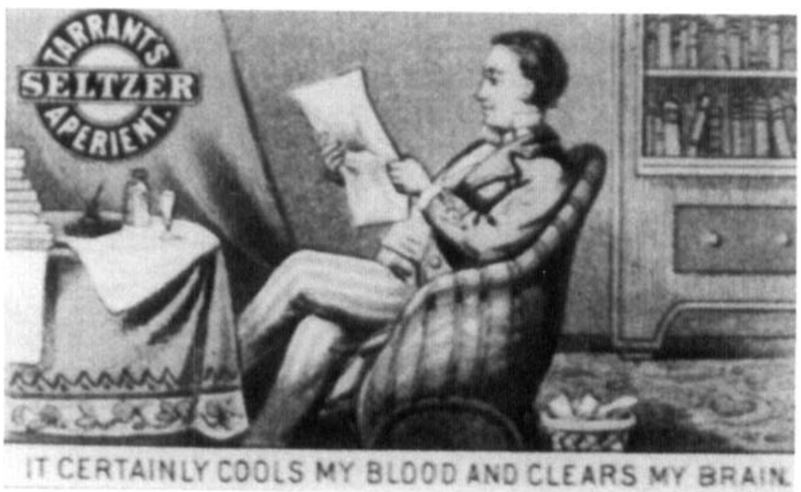


FIG. 46. Another advertisement for a "blood purifier" (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

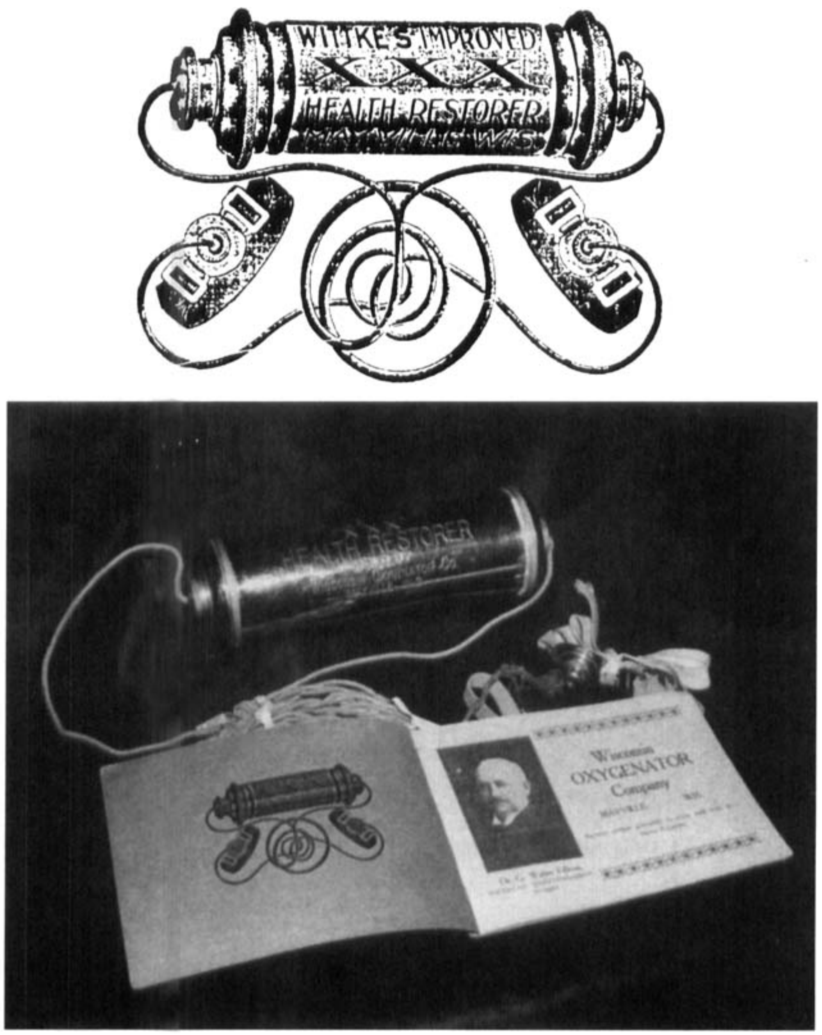


FIG. 47. (and above) Wittke's Health Restorer (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

FIG. 48. Penny arcade electric machine (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

FIG. 49. Advertisement for the magneto-galvanic "medallion" (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

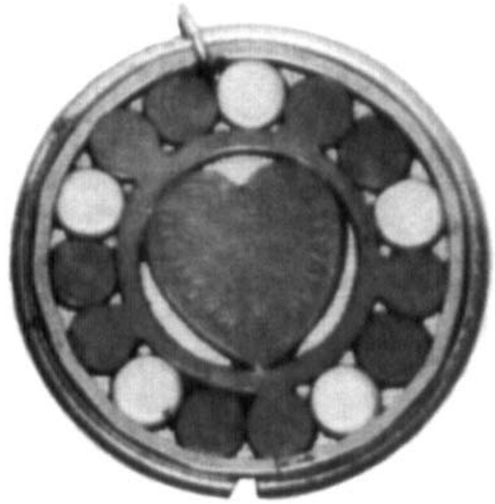


FIG. 50. The magneto-galvanic "medallion" (from the "Historical Collection of Electro-Medical and Quack Devices" of O. Lindan, Cleveland, Ohio, with permission).

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