Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Blood Transfusion In Pediatrics

Volume XI | Friday, November 3, 1939 | Number 5

STAFF MEETING BULLETIN
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Volume XI | Friday, November 3, 1939 | Number 5

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Published for the General Staff Meeting each week
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William A. O'Brien, M.D.

I. LAST WEEK

Date: October 27, 1939

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:30 p.m.

Program: Movie: "Life Begins Again"

Sulfanilamide and Sulfapyridine Therapy
Edmund B. Flink
Wesley W. Spink

Discussion
Cecil J. Watson
John L. McKelvey
Ralph T. Knight
G. Amyot
A. D. Hirschfelder
Wesley Spink

Present: 154

Gertrude Gunn
Record Librarian

- - -

II. MOVIE

Title: Society's Dog Show

A Walt Disney Short

Released by: R-K-O.

- - - -

III. ANNOUNCEMENTS

1. BABIES

Dorothy Annella Wellner daughter of Dr. and Mrs. Theodore Wellner, October 29, 1939.

Congratulations!

- - -

2. CONTINUATION STUDY COURSES

1939 (Continued)

Cardiology
November 6 - 11.

Urology
November 6 - 11.

Neurologic Roentgenology
November 13 - 15.

1940

Hospital Administration
January 15 - 20.

Dietetics
January 29 - 31.

Newborn and Premature Infant Problems (Physicians)
February 8 - 10.

Otolaryngology (Otolaryngologists)
February 19 - 24.

Medical Social Service
February 29 - March 1 - 2.

Physical Therapy Technology
March 4 - 6.

Requests for other courses have been received as follows:

Anesthesiology (Physicians)
Radiologic Technic
Nursing Personnel and Placement
Traumatic Surgery
Orthopedic Nursing
Gastro-Intestinal Surgery
Gynecology
Endocrinology
Obstetric Nursing
Pediatric Nursing
Refraction
Gynecologic Pathology
Surgical Pathology
Diagnostic Roentgenology
Roentgenologic Diagnosis (Chest)
Roentgenologic Diagnosis (G.I.)
And many others.

IV. BLOOD TRANSFUSION IN PEDIATRICS

Wallace Sako
Albert Stoesser

Blood transfusion as a therapeutic measure is no longer a major surgical problem. In fact, in recent years, it has become a routine procedure in the treatment of varied conditions. However, the indications for transfusion and the beneficial effects obtained still remain a controversial point. In the eighth annual meeting of the American Academy of Pediatrics, Berkley[1] in the round table discussion on transfusions stated that blood transfusions were given far too frequently, emphasizing the reactions, fatalities, and contraindications. The picture presented was quite gloomy. The authors have on many occasions been asked by physicians not accustomed to giving many transfusions the same question inferred by Berkley: "Why so many transfusions?". To answer this question in every instance is impossible. An attempt at evaluation of the beneficial effects of blood transfusion is frought with difficulty. Each physician has his own indications and based upon experience is entitled to his own opinion. To settle our own curiosity, we have analyzed all the transfusions performed in the Department of Pediatrics at the Minneapolis General Hospital during the years 1920 to 1939 (June 30). The age range varied from newborns up to 14 years. The transfusions were done by rotating internes under the supervision of an experienced resident. Some of the methods used in Pediatrics, physiological principles involved, reactions, as well as a brief consideratón of past and recent developments as regards transfusion are also mentioned.

EVOLUTION OF MODERN BLOOD TRANSFUSION

Blood as a therapeutic agent has been used since the dawn of medicine. The evolution of the modern method of transfusion, however, is the result of the investigations and observations of many men since the discovery of circulation by Harvey[2] in 1616. With the knowledge of asepsis and antisepsis, immunology, coagulation and anti-coagulation, blood grouping and cross-grouping, incompatibility and reactions, indications and contraindications, agglutination and hemolysis, physiology of blood and heart, and the invention of innumerable equipments, blood transfusion as a medica armamentarium has been placed on a rational and safe basis. Reactions and occasional fatalities, however, still testify to carelessness, lack of understanding, or inadequacy of our knowledge. Further study is required before one can explain the many phenomena which take place when a complex tissue like blood is transfused from one individual to another.

BLOOD GROUPS

As a result of the investigations of Landsteiner[3], Shattuck[4], Decastello and Sturli[5], Jansky[6], and Moss[7], blood from different individuals has been divided into 4 groups. Unfortunately, Moss transposed Groups I and IV of Jansky's classification, so that confusion might result from the use of the roman numerals in classification. Although in 1921, a committee of the American Medical Association recommended that Jansky's classification be followed, there are at the present time three different methods of classification used in the United States in the following order: Moss, Kansky, and International (Landsteiner). A survey of 350 hospitals in New York city by Levine and Katzin[8] disclosed that the Moss classification was used in 70%, International 23%, and Jansky 16%. These men reported the increasing use of the International method and recommended its use.

It was formerly thought that the chief requisite for compatibility be that the blood corpuscles of the donor were not agglutinated by the serum of the recipient, since the serum of the donor was so diluted that its effect on the recipient's corpuscles was nil. Recent investigations by Landsteiner and Levine[10], Belk[11], and others have shown the existence of iso-agglutinins other than those defining the blood groups,

which may lead to severe reactions and fatalities. Therefore, one must before a transfusion determine not only the blood groups of the patient and donor, but also do direct cross matching to detect presence of minor iso-agglutinins.

Polayes, Lederer, and Wiener[12] studied the agglutinogen and agglutinin contents of maternal and cord bloods in 500 cases. They found that blood groups were well defined in newborns, that cord blood did not contain agglutinins specific to mother's cells, and that 25% of 500 cases of cord bloods were incompatible with blood of their mothers due to agglutination of cells of cord blood by serum of mother and never vice versa.

USE OF UNIVERSAL DONOR

Since blood of group O (Moss IV, Jansky I) contains no agglutinogens, Ottenberg[13] in 1911 proposed the use of donors of this group as "universal donors." He thought that agglutinins A and B were sufficiently diluted in the recipient's serum to be ineffectual. Clinical experience, however, shows that severe hemolytic reactions and fatalities may occur by the indiscriminate use of the "universal donor." Levine and Mabee[14] showed that the dangerous "universal donor" may be detected by direct matching of bloods.

CAUSE OF ROULEAUX FORMATION

Rouleaux formation is not an uncommon occurrence in blood matching. Although fatalities have not occurred, marked rouleaux blood gives rise to reactions which may be undesirable. Wiltshire[15], investigating cause of this phenomenon, stated that it was quite distinct from hemagglutination, and seems certain to be due to surface tension phenomena.

CRITERIA FOR SELECTION OF DONOR

In pediatric practice, the parents are usually utilized as donors because they are most readily available. The following criteria should be used in the selection of donors.

1. Must be in good health.
2. Must be compatible.
3. Range in age from 16 to 45.
4. Sex. Males have more accessible veins and stand exsanguination better.
5. Must be emotionally stable.
6. Must be free from communicable diseases--syphilis, malaria, measles, and smallpox.

To prevent the transmission of allergy passively and to avoid protein reactions, it is customary to instruct donors not to have food within 3 hours before transfusion.

EFFECT ON DONOR

It has been shown by various workers that with 500 cc. withdrawal from healthy adult donors, no after effects result even after repeated bleeding provided that it is not done oftener than once a month. Probably the best rule to follow is to allow one week rest for every 100 cc. of blood withdrawn. Martin and Myers[16] studied the effects of blood transfusions on 10 donors and found that the average reduction in red blood count after 500 cc. withdrawal was 310,000 per cu. mm. which was regained in 4 to 6 days, the hemoglobin drop averaged 5.2% (Sahli), initial weight loss was 1.5 pound which was regained in 2 days, no change in bleeding and clotting time occurred, the blood pressure was slightly reduced but regained in 6 hours.

USE OF SAME DONOR

Repeated use of the same donor is often conducive to reactions if the blood is not carefully matched before each transfusion. In acute infections and sepsis, it is better to use different donors for each transfusion because less reaction result and better clinical response is obtained.

VIABILITY OF TRANSFUSED RED BLOOD CELLS

The length of life of the transfused red blood cells is not definitely known. Ashby[17] showed that the red cells were viable for over 30 days, Wearn, Warren and Ames[18] 59 to 113 days, and Jervell[19] over 6 weeks. Most investigators give the average viability as 30 days.

PREVENTION OF COAGULATION

There are two main procedures in preventing coagulation:

1. Rapid transfer or use of smooth surfaces simulating intima of blood vessel. Various devices have been invented to make this possible. In 1905, Carrel[20] anatomosed blood vessels of donor and recipient. Crile[21] used canula and tube, Curtis and Davis[22] paraffin coated glass tube, Lindemann[23] the multiple syringe, and Unger[24] the syringe-stopcock. The Lindemann and Unger apparatus are most widely used in pediatric practice for transfusion of unmodified blood.

2. Use of Anticoagulants. Satterlee and Hooker[25] in 1914 used hirudin. Hustin[26] in 1914 advocated sodium citrate which was popularized in the United States by Lewisohn[27]. Heparin has recently been advocated[28] because of its natural occurrence in the human body.

The Russians reported use of cadaveric blood. Skundina, Judine, Yudin and coworkers[29] found that when an individual dies suddenly--traffic accidents, electrical shock, heart attack, apoplexy, etc.--the blood rapidly coagulates at first but after a half to one and one half hours turns to a fluid state. The maximum time in which the blood remains sterile was fixed at 6 hours for summer and 8 hours for winter. A glass cannula is inserted into the jugular vein and 2 to 3.5 liters of blood collected. This blood may be kept for as long as 6 months. No toxic manifestations were encountered in over 1000 transfusions. Addition of citrate gave 20% reaction, whereas without citrate the incidence of reaction was 5%. Seven deaths occurred due to technical error. Hemoglobin rises and volume percent of oxygen rose with transfusion showing that the blood elements were functionally active.

PLACENTAL BLOOD

Rubin[30] 1914 and Goodall, Anderson, and Altimas[31] in 1938 advocated use of placental blood. The average collected was 125 cc. per placenta. As a preservative Goodall and co-workers used a citrate mixture called "citro-seroid" supplied by the Moscow Institute of Hermatology. Twenty five cc. of this mixture in 100 cc. of distilled water is mixed with 125 cc. of blood. If carefully collected, they state that cultures are not necessary because the low temperature at which the blood is preserved inhibits growth and attenuates contaminating organisms. They found the red blood cell concentration 7,000,000 or 150% that of normal adult and the coagulative power was 20 to 35% higher. Halbrecht[32] used isotonic sodium citrate as anti-coagulant and preservative. The average amount of blood collected, however, was only 50 to 60 cc. This was kept at 4 to 5 degrees C. for 14 days. Forty eight samples were tested for sterility and four contaminations with staphylococcus aureus were found. However, transfusion produced no harmful effects. One hundred sixteen transfusions were done from 520 placenta. Four reactions occurred. Page, Seager, and Ward[33] had one severe reaction in 25 transfusions.

BLOOD BANKS AND PRESERVED BLOOD

In 1918, Robertson[34] showed that citrated human blood can be bottled and preserved for as long as 26 days and be successfully transfused. The successful use of cadaveric blood by the Russians stimulated workers in the United States to find ways of preserving blood. Fantus and the Cook County Hospital[35] conceived of the blood banking idea which has now spread widely throughout the United States. Fantus stated

that for a successful operation of blood banks an average of 6 transfusions must be performed daily. He advised that blood be used within 10 days. Giddings and Kruger[36] reported analysis of 2241 transfusions of bank blood at the Kings County Hospital with an incidence of reactions of 7.3%, 0.3% contaminations and 0.4% clotting and hemolysis. No fatalities occurred. McGowin[37] studied problems connected with preservation of blood. He found that the best preservative mixture was blood 10 parts, 5.4% glucose 13 parts, and 3.2% sodium citrate 2 parts. The glucose prevented hemolysis. The potassium in the red blood cells diffused readily into plasma the first 10 days, then an equilibrium was established. The pH changed from 8 to 7 in 35 days. The red cells retained ability to respire, fragility was little changed, prothrombin of plasma was not impaired at the end of 15 days. Fantus[35] in 962 transfusions stated that the incidence of reactions increased markedly after 12 days of preservation, being 8 to 16% for blood one to 12 days old and 35 to 50% for blood 12 to 22 days old. Erickson[38] found 2% reaction with blood less than 3 days old, and 15% reaction with blood up to 21 days old. Most places now use 1.16 Grams of sodium citrate in 50 cc. of normal saline for each 500 cc. of blood withdrawn. Belenskey[39] reported that conserved blood undergoes in vitro biochemical and morphological alterations of destructive character terminating in complete loss of functional characteristics. He found less destruction occurred in dextrose-citrate solutions than in citrate-saline solutions. Cases of acute anemia or traumatic shock were less likely to have reaction with conserved blood than fresh blood. Hemostatic effect in hemorrhagic diathesis was found to be less. Preserved blood has its usefulness in convenience and in emergencies. In our practice, however, wherever possible, we have used fresh blood because less physiologic changes and less reactions occur by using fresh blood. Contrary to most reports, it is interesting to note that Lundy, Tuohy, and Adams[40] reported that in 2805 transfusions with citrated blood the incidence of reactions with fresh blood was 10.4%, whereas with refrigerated blood it was 7.8%.

METHODS OF TRANSFUSION

Today all transfusions are done indirectly. Opinion is divided as to whether modified or unmodified blood is superior and therefore should be used. In our cases citrated method was used almost exclusively except in a few cases for purposes of instruction when unmodified blood was given by the Lindemann[23] multiple syringe technique or by the Scannell apparatus[41].

CITRATE VS. UNMODIFIED BLOOD

A great deal of controversy has arisen over the relative merits or demerits of citrated over unmodified blood. The following are the criticisms advanced against the citrate method:

1. Sodium citrate is toxic. Joannides and Cameron[42] showed in their experimental studies on dogs that 0.2% citrated blood was highly satisfactory in exsanguinated dogs provided that not more than 1 gram was used which is the maximum safe dose for animals weighing between 20 to 40 pounds. They concluded that objections to the use of citrated blood as transfusion medium in cases of exsanguinated human beings are unwarranted. Salat and Wise[43] showed that toxicity of sodium citrate given intravenously into animals depended on the rate of injection. The fatal dose varied from 0.4 to 1.5 gram per kilo. Toxic symptoms began at 70 mg. per kilo. in the rabbit. They showed sodium citrate rapidly disappeared from the circulation in 5 to 10 minutes, after intravenous injection into cats and dogs. Cheer[44] and Gechner[45] showed in animal experiments that citrated blood even in concentrations of 0.4 to 0.5% was not toxic.

Evidence both experimentally and clinically seems to indicate that sodium citrate as usually used in transfusions (0.27%) is non-toxic. As Lewisohn[46] has pointed out the incidence of reactions with citrate is no higher than with unmodified blood if equal care as to details of technique is applied. Our ex-

perience confirms this statement.

2. Calcium Immobilization. Our observations on 10 cases showed that following citrated blood transfusion in dosage of 20 cc. per kilo in children, the serum calcium is normal and the clotting time of the blood is not affected. Mellon, Hastings, and Casey[47] stated that the purpose of citrate is to render calcium unavailable for formation of thrombin probably by tying it up in some undissociable form.

3. Disturbances in hydrogen-ion concentration of blood. McGowin[37] showed that pH of citrated blood stored for 35 days changed from 8 to 7.

4. Injury of platelets. Herr[48], Agnew[49], Belensky[39] and Unger[50] have stated that the blood platelets are injured or destroyed. On the other hand Lewisohn[46], Lewisohn and Rosenthal[51], Gechner[45], and others showed that with usual dose of citrate, platelets behave normally and are not diminished.

5. Changes in fragility of red cells.

6. Immobilization of white cells.

7. Alteration of hemostatic powers of blood.

8. Development of anticomplementary properties of serum.

9. Alterations in immunological reactions of blood in respect to antitoxic, virucidal, bactericidal, and other antibody properties.

All these arguments have been advanced against the citrate method, by various authors, chief among whom are Unger[50], Belensky[39], Bacon[52], Drinker and Brittingham[53], etc.

The proponents for the citrate method have been chiefly Lewisohn[46], Weil[54], McGowin[37], and others who argued that citrated blood did not increase fragility of red cells, that it did not diminish available quantity of complement in blood, and did not diminish phagocytic power of the white cells or induce biochemical alterations of destructive character. In short, they found no evidence that the protective power of blood was in any way interfered with.

In spite of the unfavorable reports of citrated blood transfusion, the fact still remains that it is the most popular method in this country today. Its flexibility and convenience offset any argument that whole blood is more physiological. The skill of the operator and minimal disturbance of the patient is of far greater importance than the merits of one method over another. Clinical evidence suggests that fresh citrated blood is to be preferred over conserved blood except in emergencies.

AMOUNT OF CITRATE USED

Ten cc. of 2.5% sodium citrate per 100 cc. of blood is used which makes a concentration of 0.27% concentration of citrate.

ROUTES OF TRANSFUSION

1. Intravenous.
   - A. Antecubital. In older children.
   - B. Scalp. In infants.
   - C. Internal saphenous at ankles. Place of choice in exposig a vein.
   - D. External jugulars.
   - E. Superficial veins of foot or dorsum of hand.
   - F. Femoral vein.
2. Cutting down. The place of choice is the internal saphenous at ankles.
3. Intrasagittal. Helmholz[55] in 1915 advocated the sagittal sinus as place of preference in infancy.
4. Intraperitoneal. Siperstein and Sansby[56] showed that in rabbits,

the red cells are absorbed when injected intraperitoneally. Sansby and Siperstein[57] stated that intraperitoneal transfusion of citrated blood gives good results in anemia. No harmful effects were observed in 50 cases. However, its use in severe nutritional disturbance was questionable. They stated that the procedure was harmless, but this is seriously questioned by most pediatricians. Cunningham[58] showed that blood cells passed through walls of lymphatics in diaphragm. Our experiences in 6 cases, two of whom came to autopsy, showed the blood very little absorbed at the end of 9 and 14 days respectively. The procedure is unsound surgically and absorption is not dependable. Both these factors mitigate its use.

5. Intramuscular. The intramuscular administration of blood has its usefulness in prophylaxis against communicable diseases, but otherwise the effect obtained cannot in any way measure up to the response obtained with introduction of blood directly into the circulation.

AMOUNT OF BLOOD TO TRANSFUSE

In infants, 20 cc. of blood per kilo is well tolerated. In older children 10 cc. kilo is the usual dose. Halbertsma[59] stated that 15 cc. kilo produced a rise of 1 million red cells in anemic children. Krahulik and Koch[60] recommended modification of Young's rule for dosage of drugs: $\frac{\text{Wt.}}{\text{Wt.}+40} \times 500 =$ amount of blood to transfuse.

EQUIPMENT MOST USED

1. Citrate + gravity.
2. Citrate + Unger stopcock-syringe method. Most frequently used in infants.
3. Citrate + cutting down of internal saphenous vein at ankle.
4. Citrate + Lindeman multiple syringe method.
5. Unmodified blood + Lindeman multiple syringe method.
6. Unmodified blood + Scannell apparatus.

SPECIAL TYPES OF TRANSFUSIONS

1. Autotransfusion. This method is not practical in pediatrics.

2. Exsanguino-transfusion. Robertson, Brown, and Simpson[61] stated that the rationale of this procedure is that the withdrawal of blood mechanically removes a certain amount of circulating toxins or bacterial infection and makes room for its replacement by fresh non-toxic blood containing fresh complement' and possibly immune bodies present in normal adult blood. This procedure has been most frequently used in cases of septicemia and toxemia. Robertson[62] in 1921 advocated and used it with good results in the treatment of severe burns in infants and children. Lantin and Guerrero[63] reported good results in treatment of 41 cases of typhoid fever. It has also been used in various forms of poisoning. It seems to us, however, that the risk to a child is too great to advocate this procedure over that of ordinary transfusion.

3. Immunotransfusion.

   A. Specific. In 1919, Wright[64] advocated use of donors who had been previously artificially immunized with specific organism causing infection in the patient. This procedure takes too long and is not practical in diseases running a short course. Brody and Crocker[65] report good results in the treatment of septicemia.

   B. Non-specific. This procedure is simpler and more rapid, consisting of immunizing donors with non-specific vaccine. It is based on the principle of increasing the formation of non-specific antibodies or opsonins in the donor's blood. Fry[66] using streptococcus-staphylococcus vaccine in septicemia and wound infections stated that favorable results can be attributed to: (1) antibacterial mass action,

(2) protein shock therapy,
(3) sensitization to vaccine,
(4) replacing hemolyzed red cells. Bradford[67] using anti-pertussis immunized blood stated that it is effective in prophylaxis and during the incubation period but not during the disease. Barach[68] reported on favorable results in pneumonia. Habel and Cooke[69] observed that in typhoid fever opsonins and non-specific immune bodies are increased. Gill[70] had good results in septicemia of otolaryngeal origin.

4. Irradiated Blood. Hancock and Knott[71] in 1934 irradiated blood and then transfused. Each 10 cc. of blood was irradiated with ultra-violet light for 30 seconds. They stated that beneficial effects may be due to: (1) coagulation of bacteria creating an autogenous vaccine, (2) increase in germicidal properties of blood and antibodies, (3) secondary radiation causing stimulation of individual cells, hematoblast cells, and endocrines, (4) increase in vitamin D content of cholesterol and plasma, (5) increase in oxygen absorption of blood.

5. Convalescent Blood

In the field of contagious diseases, convalescent blood often brings about rapid improvement with fall in temperature by crisis. This occurs with or without anemia. The immune body content of blood has been determined at various times but it has always been found to be less than the therapeutic sera which are on the market. However, in respect to safety and clinical response obtained, convalescent blood has certain advantages. Good results have been reported with use of this procedure in scarlet fever, pertussis, erysipelas, undulant fever, measles, mumps, and chickenpox. Its value in poliomyelitis is debatable, although it has been extensively used in the prophylaxis and treatment of this disease.

REACTIONS AND COMPLICATIONS

Polayes and Lederer[72] listed the cases of blood transfusion reactions as follows:

1. Incompatibility between donor's and recipient's blood due to:

   A. Errors in grouping blood due to:

      (1) Poor or wrong technic.
      (2) Use of low-titered or contaminated test serum.
      (3) Weak agglutinins or agglutinogens in recipient's blood.
      (4) Pseudo-agglutination.
      (5) Auto-agglutination and cold agglutination.
      (6) Anomalous or atypical agglutination; subgroups.
      (7) Contamination of recipient's blood by bacteria.
      (8) Effect on blood groups of drugs.

   B. Indiscriminate use of universal donor.

   C. Immune iso-antibodies and hemolysins.

2. Unclean apparatus.

3. The use of sodium citrate solution.

4. Incipient coagulative changes in the transfused blood.

5. Allergic reactions in recipient.

6. Systemic disease in recipient. Overtaxing heart and kidneys.

7. Transmission of disease to recipient. measles, malaria, smallpox, syphilis.

8. "Speed shock."

9. Embolism.

Speed shock has been mentioned in the literature[73] but we have not encountered a case where this has occurred, although in some children transfusion was accomplished in 10 minutes. However, we have wherever possible given the blood by the slow drip method at the rate of 30 to 60 drops per minute.

Fell[74] lists four main types of reactions: (1) shock and renal suppression

due to incompatibility, (2) chills and fever due to protein reaction, (3) hyperthermia, (4) allergic.

DeBakey[75] as a result of experiences in 1500 transfusions of unmodified blood stated that the chief difficulties with this type of transfusion were: (1) agglutination, (2) coagulation, (3) infection, (4) introduction of needles, (5) clotting in needles and tubing, (6) clotting in conveying intermediary.

DeGowin[76] listed 13 grave sequelae occurring in 3500 transfusions as follows:

1. Renal insufficiency due to incompatibility -- 7 cases. Alkalization of urine before a transfusion is claimed to protect the kidneys from excreted hemoglobin if hemolysis occurs. Five deaths occurred in this group.

2. Hemolytic reaction without renal insufficiency -- 5 cases.

3. Retinal hemorrhage -- 3 cases.

4. Pulmonary edema -- 2 cases with 2 deaths.

The incidence of reactions and fatalities reported by various authors is summarized in Table I.

TABLE I. INCIDENCE OF TRANSFUSION REACTIONS, COMPLICATIONS, AND FATALITY REPORTED IN THE LITERATURE

Author and Year Reported	Number of Transfusions	Number of Patients	Type of Blood	Incidence of Reactions		Complications Number	Fatality		
				Number	Per Cent		Number	Per Cent	Cause
Our Series (1939)	1846	827	Citrate 1678 Unmodified 168	29	1.6	Infection 2	2	0.10	Pulmonary edema 1 Sinus Transfus. 1
DeGowin[76] (1938)	3500	-	Citrate	-	-	Renal insufficiency 7 Hemolytic reaction 5 Retinal hemorrhage 3 Pulmonary ed. 2	7	0.20	Renal insufficiency 5 Pulmonary edema 2
Giddings & Kruger[36] (1939)	2241	-	Citrate preserved	164	7.3	-	0	0	-
Fantus[35] (1938)	962	-	Citrate preserved	130	13.5	-	0	0	-
Lewischn[46] (1937)	723 including children	-	Citrate	-	1.5	0	0	0	-
	653 adults only	-	Citrate	-	1.2	0	0	0	-
Lundy, Tuohy, Adams[40] (1938)	2805	-	Citrate Fresh 782 Refrig. 2023	- - -	9.7 7.8 10.4	-	0	0	-
Andrus[89] (1937)	634	-	Citrate	-	13	-	0	0	-
Allen[90] (1938)	?	150	Citrate	?	?	?	1	?	?
Levine & Katzin[9] (1938)	?	? 350 Hosp.	Mostly citrate	?	?	60	16	?	
Bernheim[91] (1921)	?	?	Citrate unmodified	- -	40 5	?	?	?	?

TABLE I. INCIDENCE OF TRANSFUSION REACTIONS, COMPLICATIONS, AND FATALITY REPORTED IN THE LITERATURE (Continued)

Author and Year Reported	Number of Transfusions	Number of Patients	Type of Blood	Incidence of Reactions		Complications Number	Fatality		
				Number	Per Cent		Number	Per Cent	Cause
Meleneg, Stearns, et al[92] (1917)	280	99	Citrate 196 Unmodified 73	127 47	65 65	?	?	?	?
Unger[93] (1917)	165	128	Citrate Unmodified	- -	57 3	?	?	?	?
Berkley[1] (1939)	1800	?	Citrate & Unmodified	?	?	?	24	1.3	
Powers[94] (1937)	313	-	Citrate	-	4.5	-	0	0	-
Fell[74] (1938)	500	288	Citrate 18 Unmodified 482	58	17.6	-	0	0	-
Blain[95] (1929)	3000	-	Unmodified	10	0.3	-	0	0	-
DeBakey & Harrold (1938)	1500	-	Unmodified	-	0.5	-	-	-	-
Sloan[96] (1921)	436	-	Unmodified	-	5	?	?	?	?
Halbrecht[32] (1939)	116	-	Placental citrate	4		?	0	0	-
Polayes & Morrison[97] (1932)	1500	1000	Unmodified	-	2.8	?	9	0.9	-
McClure & Dunn[98] (1917)	150	80	?	45	30	?	2	1.3	-

CAUSES OF FATALITY

The chief cause of fatality is carelessness. Among the specific causes mentioned in the literature are:

1. Renal insufficiency due to incompatibility.
2. Pulmonary edema.
3. Cardiac failure.
4. Accidents.

PHYSIOLOGY OF BLOOD

Blood is a complex tissue with manifold functions much of which is not yet clearly understood. It acts as a nutritive medium to all the tissues and organs of the body transporting food and oxygen to them and carrying away their waste products, carbon dioxide and nitrogenous material, to the excretory organs such as the skin, lungs, and kidneys. Under normal conditions the blood composition varies from time to time but the various organs of the body are able to take care of such changes. Under pathological conditions, however, changes may be so great that the organs are unable to undergo adjustments. Various disease conditions may upset the intimate balance which exists between the cellular elements, plasma, and tissue fluid.

PHYSIOLOGICAL EFFECTS OF BLOOD TRANSFUSION ON THE PATIENT

The various physiological effects which may be obtained by blood transfusion may be tabulated as follows:

1. Supplies fluid bulk. It has long been realized that in such conditions as surgical shock, isotonic salt solutions are of very little value because they do not remain in the vascular system long enough. Gumacacia having the same osmotic pressure as blood is somewhat effective in this regard but reactions and fatalities have resulted too frequently, and physiologically is not as ideal as blood.

2. Supplies cellular elements, leucocytes, erythrocytes, and platelets, thus increasing body defenses, oxygen carrying capacity, and coagulation of blood.

3. Supplies colloids and electrolytes, thus restoring osmotic pressure, hydrogen ion concentration, and irritability and stability of tissues.

4. Supplies immunologic elements such as antibodies and opsonins.

5. Stimulates various tissues such as hemopoiesis in the blood forming organs.

6. Other physiological effects unknown at present time.

BLOOD VOLUME OF NORMAL CHILD

Gallerani[77] studied blood volume of 92 normal children by the trypan red method. He found that the total blood volume averaged 60 to 90 cc. per kilo of body weight, the mean for the boy being 80.8 and for the girl 73.6. In males this was 0.086 of their body weight and in females 0.081 of body weight.

SHOCK

In shock there is a loss of fluid from the blood and exudation of colloids into the tissues. The administration of hypertonic glucose solution may help temporarily, but the ideal and most physiologic treatment is the administration of blood. Often large amounts of blood are necessary by continuous infusion.

HEMORRHAGE

Eyster and Middleton[78] showed that hemorrhage and transfusion of blood in man in amounts within 1% of the body weight result in only transitory alterations of cardiac size and blood pressure. Compensatory mechanisms cause a rapid readjustment to normal circulatory conditions notwithstanding the altered blood volume.

DIARRHEA

Cooper[29] has shown that with acute diarrhea the serum protein, blood chloride

and non-protein nitrogen is elevated but with chronic diarrhea the non-protein nitrogen is normal but serum protein and blood chloride is low. In the former case, water leaves the blood rapidly resulting in anhydremia, whereas in latter condition the fluid remains in the blood much longer.

ANESTHESIA

Searles[80] showed that ether causes concentration of blood due to exudation of fluid into tissues and also causes the spleen to contract putting out reserve of blood elements. Stewart and Rourke[81] showed that ether anesthesia for one to 3 hours reduces blood volume 13.4%. Consequently, there is rationale for fluid administration before surgery, and transfusion post-operatively or during surgery.

ANEMIAS IN CHILDREN

Since anemia plays such a prominent part in pediatric practice, a detailed discussion is presented. The term may be defined as any state in which the hemoglobin is in less than normal proportion to the blood volume. The number of the red cells may or may not be reduced in proportion to the hemoglobin deficit. Such a condition can arise from some one of the following causes:

1. Direct blood loss, acute or chronic.

2. Failure of red cell formation.

   A. Hypoplastic states of bone marrow. By this term is meant a condition in which the erythropoietic activity of the marrow is for the time being partially or completely suspended, although capacity for function is still present, and when the cause of the hypoplasia is removed, return to normal is to be expected. This state is the chief factor in the production of many of the secondary anemias of childhood, particularly those due to infection in which the toxins of the infectious process have a depressing effect on the marrow. This condition also accounts for anemia accompanying malnutrition in which the general metabolic level is low and marrow function is manifested by anemia with lack of the ordinarily recognized signs of red cell regeneration.

   B. Aplastic states. The term aplasia is generally used to indicate the destruction of so much of the marrow that red cells sufficient for the body's needs can no longer be produced. Such marrow destruction can be caused by poisons, physical agents such as X-rays and radium, septic processes, leukemia, Hodgkin's disease and malignancy.

   C. Lack of structural material.

3. Excessive red cell destruction. This occurs in severe infections, hemolytic icterus, and poisoning.

4. Lack of hemoglobin formation due to lack of iron and other constituents.

5. A combination of 2 or more of above factors.

NUTRITIONAL ANEMIA

Nutritional anemia is due to lack of some substance in the diet so that hemoglobin formation cannot occur normally. It has long been observed that breast fed infants show a tendency toward anemia unless additional iron is administered. Dewaney[82] following the hemoglobin in breast fed infants found that the hemoglobin at birth averaged 120%, at end of second week 96%, second month 76%, sixth month 68%, twenty-fourth month 65%. In other words, there was a tendency toward low hemoglobin level from the second month up to the end of the second year after which it slowly rose again. Nutritional anemia of short duration responds well to iron and adequate diet, but if of long duration the response is not so good. Parson and Wright[83] showed that chronic anemia causes dilatation and hypertrophy of the heart. Other evidences also indicate hypoplasia of the blood forming organs. If the anemia persists long enough the cardiac and hemopoietic damage may become irreparable.

ANEMIA IN INFECTION

The association of anemia with infection is a common phenomena. The mechanism by which anemia results is not entirely clear but it probably is a combination of nutritional factors together with toxic effect upon hemopoietic apparatus or blood elements. Domeshek and Shwartz[84] in experimental studies stated that spherotocytosis and increased fragility of the red cells in hemolytic anemia may be due to the activity of an hemolysin rather than to defective formation of the red blood cells in the bone marrow.

Infective processes induce marrow hypoplasia which if prolonged lead to marrow decompensation. Marrow recompensation may occur if the contributory factors are eliminated. Meanwhile blood transfusion helps in preventing permanent damage to the heart and hemopoietic system. Our experiences have shown that anemia resulting from toxin or infection does not respond well to iron administration. Sussman[85] showed that with infection there is a progressive fall in the hemoglobin. Repeated small transfusions can maintain the hemoglobin at the normal figure. In acute infections he stated that three beneficial results may be derived from transfusions: (1) Replenishment of hemoglobin and red blood cells, (2) Introduction of immune bodies, (3) Bone marrow stimulation. Experimentally it can be established that large transfusions in anemia depress bone marrow function. In children, however, transfusion of 10 to 20 cc. blood per kilogram of body weight stimulates bone marrow as evidenced by increase in reticulocytes.

TOXICITY OF HEMOGLOBIN

Ottenberg and Fox[86] showed that 3.45 to 8.25 grams of hemoglobin injected intravenously into 20 normal individuals caused no untoward reactions.

BEHAVIOR OF HEMOGLOBIN AFTER TRANSFUSION

Sibley and Lundy[87] showed that the average rise in hemoglobin following a transfusion of 500 cc. of citrated blood was 1.5 grams of hemoglobin per 100 cc. This rise was manifested about 2 days following the transfusion, and gradually decreased thereafter, reaching about 1 gram increase in 10 days. In cases in which no reaction occurred, the rise in hemoglobin was 2.12 to 2.8 grams per 100 cc. In cases with a reaction the increase in hemoglobin was approximately 50% loss on average. The lower the value of hemoglobin of recipient before the transfusion, the greater the amount of increase in value for hemoglobin after the transfusion.

SINGLE OR REPEATED TRANSFUSIONS

In our experience, repeated small transfusions have given better results than one large transfusion in the anemias. It was also observed that early rather than late transfusion gave the maximum benefit. With hemoglobin less than 30% (Sahli), a large transfusion often causes alarming reactions. In such instances not more than 5 cc. per kilo of blood should be given.

ANEMIA WITH HEMORRHAGE AND BLOOD DYSCRASIAS

There does not seem much argument that transfusion is indicated in these conditions. In an invariably fatal disease such as leukemia and Hodgkin's, many feel that transfusions are not indicated. If such be the case, then on the basis of the same argument we should not treat hopeless cardiacs, malignancy, cerebrospastics, mongols, etc.

ATHREPSIA

In this condition which is not uncommonly encountered in pediatric practice, blood transfusion increases blood flow, blood volume, and protein, with often marked improvement in the condition of the patient.

ALIMENTARY INTOXICATION

In this condition vomiting and diarrhea plays a prominent picture. Dehydration, alkilosis, or acidosis results. Proper administration of electrolytes brings prompt relief in many instances. In other instances, the administration of blood in conjunction with electrolytes may be necessary.

ANALYSIS OF 1846 TRANSFUSIONS ON 827 CHILDREN

No sera or antipyretics were given prior to or within 24 hours after transfusion. In the citrate transfusion, 15 cc. of 2% sodium citrate was added to every 100 cc. of blood. The transfusion was done largely by residents who were experienced in the procedure, or by internes properly supervised by an experienced resident. The results are summarized in more or less outline form in order to conserve space and for the sake of clearness.

Number of children transfused 827

Number of transfusions 1846

Age Groups:

Newborns up to 2 years	273	transfusions
2 to 5 years	186	"
5 to 9 years	197	"
9 to 14 years	176	"
Total	827	"

Reactions and Complications:

1. Fatality:

Pulmonary edema	1
Sinus transfusion	1
Total	2 (0.24%)

2. Infection at site of injection 2

3. Transfusion reaction:

Chills alone	3
Hyperthermia or chills or both	26
Total	29 (1.6%)

Type of Blood Transfused:

Unmodified	168
Citrated	1678
Total	1846

Routes of Transfusion:

Intraperitoneal	6
Intravenous	1640
Sagittal sinus	33 (1 death-3%)

Apparatus Used in Order of Frequency at Different Age Periods:

0 - 2 years

Unger
Lindeman
Cutdown:
1. Unger
2. By gravity

2 - 5 years

Unger
Gravity
Lindeman

5- 9 years

Gravity
Unger
Lindeman

9 - 14 years

Gravity
Unger
Lindeman
Scannell

Veins Used in Order of Frequency at Different Age Periods:

0 - 2 years

External jugular
Scalp
Internal malleolus
Foot and Hand
Antecubital
Sinus
Femoral

2 - 5 years

Antecubital
External jugular
Scalp
Internal malleolus
Foot and Hand
Femoral

5 - 9 years

Antecubital
External jugular
Foot or Hand
Scalp

9 - 14 years

Antecubital
Internal malleolus

Indications at Time of Transfusion

In the criteria for calling a case as anemia we have set the arbitrary level of 60% (Sahli) as the lower limit of normal. The normal hemoglobin of healthy children in Minneapolis was found to be about 85% (Sahli) in going over the records of 100 children.

1.	Primary anemia	17
2.	Hemolytic anemia	25
3.	Nutritional anemia	47
4.	Hemorrhage	36
5.	Blood dyscrasias	18
6.	Acute contagious diseases	169
7.	Acute non-contagious diseases	128
8.	Chronic infections	68
9.	Pre-operative	47
10.	Post-operative	79
11.	Malnutrition	33
12.	Intoxication	37
13.	Shock	30
14.	Sepsis	52
15.	Diarrhea, vomiting	36
16.	Nephrosis	5
	Total	827

Under intoxication is listed:

Burns	21
Poisoning	8
Uremia	8

Association of Anemia with Infections:

1. Acute contagious diseases:
   Anemia present in 51 (30%).

2. Acute non-contagious diseases:
   Anemia present in 42 (33%).

3. Chronic infections:
   Anemia present in 48 (56%).

COMPARISON OF EFFECT OF IRON AND TRANSFUSION IN ELEVATING HEMOGLOBIN

Ten cases of nutritional anemia were treated by iron or iron and copper in association with diet. The hemoglobin ranged from 30% to 50%. Average time it took for the hemoglobin to rise to normal in these two cases was 32 days.

There is a controversy at present as to whether transfusions are indicated in nutritional anemia. The exact mechanism in nutritional anemia is not entirely clear. That iron alone is not the chief factor is attested by failure to respond to iron in several instances. Anemia predisposes to infections. At least in our series of 47 cases, most cases gave repeated history of upper respiratory infections. Infections definitely lower hemoglobin due either to toxic effect upon bone marrow or direct action on blood elements. Stimulation to hemopoiesis requires an adequate oxygen carrying capacity of the red cells. With anemia, the oxygen carrying capacity is reduced, and therefore, hemopoiesis is diminished. Thus a vicious circle is established, anemia leading to susceptibility to infections, and infections predisposing to anemia. The child looks pale, lacks appetite, and therefore the administration of an adequate diet is difficult even in the hands of an experienced nurse. It is, therefore, too much to expect mothers of these indigent charitable cases to feed these children with an adequate diet. Transfusion or a series of transfusions brings about a rapid rise of hemoglobin to normal level, normal pink color to cheeks, brightness and normal activity, and return in appetite.

BEHAVIOR OF HEMOGLOBIN FOLLOWING TRANSFUSION IN ANEMIAS

1. Rise of Hemoglobin in Primary Anemia: 17 cases.

Five cases of aplastic anemia were followed and average rise of hemoglobin following 20 cc. citrated blood per kilogram of body weight was 15%. On the whole as the hemoglobin rose, the degree of rise became less so that when 80% was reached rise was only 5%.

2. Rise of Hemoglobin in Nutritional Anemia: 47 cases.

Following a transfusion there was a prompt rise, the degree of rise depending on the level of hemoglobin prior to transfusion. Following 20 cc. per kilo transfusion the hemoglobin rise was as follows:

Hemoglobin prior to transfusion			20%	------	Rise of	30% (Sahli)
Hemoglobin	"	"	30%	------	"	" 28%
Hemoglobin	"	"	40%	------	"	" 25%
Hemoglobin	"	"	50%	------	"	" 20%
Hemoglobin	"	"	60%	------	"	" 15%
Hemoglobin	"	"	70%	------	"	" 7%

The maximum rise in hemoglobin occurred in 3 days. At the end of 7 days, it was approximately 60% of rise at end of 3 days.

The behavior of the hemoglobin post-hemorrhage was similar to above provided hemorrhage did not persist.

3. Rise of Hemoglobin in Anemia Associated with Acute Infections.

No constant curve for rise in hemoglobin was obtained in 131 cases. The degree of rise depended upon the severity of the infection, the level of hemoglobin prior to transfusion, and on whether hemolytic factor was associated with infection. With active infection daily transfusion can raise hemoglobin to normal level provided hemolytic factor was not present. However, it was very seldom that the hemoglobin could be elevated above 80% in the presence of active infection in spite of daily transfusions. Maximum rise in hemoglobin occurred 12 hours following a transfusion, this was maintained for 2 days, after which the hemoglobin tended to drop rapidly again, so that the original level of hemoglobin was obtained at end of 4 days. Therefore, in the presence of an acute infection, transfusion at least every 2 days is necessary to maintain hemoglobin level.

4. Rise of Hemoglobin with or without Reaction.

Chills or fever or both had no effect in hemoglobin rise, unless hemolytic factor was present. When hemolysis occurred the rise was not dependable. In sickle cell anemias and hemolytic anemias of newborn, there often occurred a fall in hemoglobin although blood was compatible on ordinary matching.

TRANSFUSION IN LOBAR PNEUMONIA

Berkley[1] stated that anemia or lack of blood volume is rarely a problem in pneumonia, and that transfusion in pneumonia is rarely if ever good therapy and often is most harmful. Eleven deaths out of 24 occurred as a result of acute heart failure. Nine of these eleven were due to "speed shock." He found that anemia very seldom occurs in pneumonia. He summarized by stating that "transfusion in pneumonia may be and often is worse than useless." Our results as well as the reports of others[88] do not agree with the statements of this author.

We have analyzed 74 cases of lobar pneumonia who were transfused during the acute febrile stage and the results are tabulated in outline form. No deaths occurred with these transfusions, nor were evidences of speed shock or cardiac failures noted in these cases.

	Temperature Drop By Crisis	No Crisis
Lobar Pneumonia with Anemia	17	11
Lobar Pneumonia with Anemia	22	14
Total	39 (53%)	25 (47%)

Incidence of anemia in lobar pneumonia - - - - - - - - 28 (38%)

ANALYSIS OF TRANSFUSION IN ACUTE CONTAGIOUS DISEASES

	Crisis	No Crisis
Scarlet Fever	12	34
Pertussis	9	17
Measles	16	39
Chickenpox	6	6
Erysipelas	2	7
Mumps	2	3
Poliomyelitis	0	32

In these cases, as far as possible, donors were utilized who gave a history of having had the disease in childhood. Cases transfused with convalescent blood are not included in this series except that for poliomyelitis. In many instances, it was noted that one transfusion brought marked improvement with immediate drop in temperature, followed by a rise again. In these cases whenever transfusions were repeated temperature dropped again and remained so as long as the transfusion was repeated.

SUMMARY AND COMMENT

1. Modern blood transfusion is a comparatively safe procedure. Practically all fatalities today can be attributed to carelessness or failure to utilize the knowledge we now possess as regards blood transfer.

2. The citrate method was found to be the safest and most practical for children.

3. The route and method employed are governed by two principles:

A. That a maximum of safety and benefit be conferred to the patient.

B. That a minimum of disturbance be created in the patient by the procedure. When judged by such principles, sinus and intraperitoneal administration of blood is not practical for routine use.

4. The indications for transfusion are not always clear cut. The ultimate guide vests with the beneficial results which one wishes to confer to the patient.

5. The dosage of blood which can be safely transfused at one time depends on the weight and condition of the patient. In acute hemorrhage, an amount equal to the volume lost may often be offered. In most instances, the average was 10 cc. per pound of body weight. In anemia with a hemoglobin or red count below 50% of normal, not more than 5 cc. per pound should be administered; larger amounts may precipitate a severe reaction or cardiac embarrassment.

6. Preserved blood has its indication in hemorrhage or emergencies; otherwise, fresh blood has given better results and less reactions.

7. Iron deficiency or nutritional anemia was difficult to separate from anemia which results from repeated upper respiratory or gastro-intestinal infections. Often one cannot be sure whether infection or dietary lack originally set the stage for the anemia. Once a vicious cycle is established between nutritional deficiency, anemia, and infection, the administration of iron alone was

found ineffective, whereas blood transfusion gave a prompt beneficial response.

8. The incidence of anemia in infections was high, contrary to popular opinion otherwise. In this type of anemia, repeated small transfusions were more effective than a single massive transfusion. To prevent hemoglobin or red cell count from dropping, blood must be administered at least every three days during the active stage of a severe infection.

9. Early transfusion gives the maximum benefit under any circumstances; blood administered during the terminal stages of a disease, which prone to do, was found to do very little good and may precipitate deaths.

10. Analysis of our cases reveals that a plea for less transfusion voiced by many should be supplanted by a plea for careful, early, and repeated transfusions in cases with proper indications.

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V. GOSSIP

Last week's staff meeting on Sulfanilamide and Sulfapyridine Therapy drew the largest crowd of the present series. The intense interest in the subject is evident. Dr. Flink presented the contribution of Drs. Flink and Spink in admirable fashion. The warnings in regard to indiscriminate therapy with these drugs was repeated over the radio in celebration of National Pharmacy Week. This Week, magazine section of the Minneapolis Tribune, October 29, 1939, carried a splendid popular article on Sulfanilamide - Miracle or Menace? by Surgeon General Thomas Parran. According to the author, the people of the United States consumed 187 tons of sulfanilamide last year. Furthermore, he points out "that this drug which has cured or relieved thousands of persons suffering from at least 20 different serious diseases is highly dangerous if misused." The article should be read....Speaking of the character of Jeeter in "Tobacco Road," who opens his paw's coffin before placing it in the grave and discovers that rats in the night had knawed on the cadaver reminds me of a believe-it-or-not up here in Minnesota. He was discharged from the hospital to a rest home. There he grew lonely for his own place, a miserable bachelor shack which had been unattended since his illness. One night the homing instinct became so strong that he departed without sufficient clothing. He was cold when he arrived and went to bed without starting a fire. During and night and morning, he grew weaker and at some time during the day or night "shuffled off." When the body was found, the rats had made a meal of his features. ...Chief dermatologist, Henry E. Michelson, departs next week for Philadelphia to take part in the second annual meeting of the American Academy of Dermatology and Syphilology to be held at the Bellevue-Stratford Hotel. The president is Paul A. O'Leary of the Mayo Foundation. Dr. Michelson will give a series of clinics and luncheon discussions. The arrangement of the program is similar to that of the ophthalmologists and otolaryngologists. Otolaryngologist Erling S. Hansen, the most accomplished dialect comedian of our staff, has been made secretary for public relations of the American Academy of Ophthalmology and Otolaryngology. In his new position, Dr. Hansen should be able to bowl over the opposition by "going into character".... The Hallowe'en Party on fourth floor peds was an outstanding success, thanks to the efforts of Dorothy Jones and her associates. 55 children walked, hobbled, or were carried to the affair. The movies were greatly appreciated (many, including some of the older children, had never seen movies before). They had a regular program, with songs by Elizabeth Richardson, readings by Margaret Fischer, and violin selections by Pearl Howdeshell. The children played games and all had a chance at the fishing pond. The refreshments were in keeping with the day, and at four o'clock the party finally broke up as the children went back to their beds in the various sections. For many, it will be the happiest remembrance of their lives. Miss Jones insists that Marguerite Donker, the Dutch girl with the blond braids and the blue eyes, should receive major credit for the party. Everyone who was able to help did so, and a happy Hallowe'en was had by all....In the Berlin letter in the Journal of the American Medical Association (October 21, 1939) there is the story of the Congress of Surgeons. Several sections are of interest: "The efforts of neurologic surgeons to organize a distinct group was thwarted only by ministerial interference and by uniting them into a subdivision of the society," "Roentgenology is not a separate specialty but a medical ally," "Lehmann thinks that the x-ray department of a hospital should be in charge of a roentgenologist who is subject to the director of the surgical division," "A motion to organize special tumor clinics in Germany did not meet with the approval of the society."....The following report was received at the Superintendent's Office, "Patient was very drowsy - had been irrational at times last evening. Got out of bed to void, she says. Thought she was at home. Found standing at bedside. Dr. K. on the floor at the time....