

# MEDICAL BULLETIN



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Hemorrhagic Hypotension*

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## Staff Meeting Report

### Determination of the Blood Flow by a Radiographic Technique\*

Sadek K. Hilal, M.D.,† and Kurt Amplatz, M.D.‡

**B**lood flow has long been an interesting and an important subject because of its physiologic, pathologic, and clinical implications. It is therefore not surprising that since the turn of the century numerous methods have been devised to measure blood flow.<sup>1,2</sup> These techniques use a variety of principles, such as the dilution of indicator, the Fick principle, the measurement of the electromagnetic fields, the propagation of ultrasonic waves, and many other biophysical phenomena.<sup>3-9</sup>



SADEK K. HILAL.

The radiographic technique is essentially an indicator dilution method. The radiopaque indicator is injected in the artery at a known constant rate, and its dilution by the blood stream is determined simply by the measurement of the optical density on the radiograph. Obviously, the variation of the concentration of the opaque medium is reflected as a darker or lighter image on the radiograph. The flow is determined by the Hamilton-Stewart formula from the known rate of injection and the radiographically measured dilution of the opaque substance:

$$\text{Flow (Liters/min)} = \frac{\text{Amount of dye injected/Min. (cc/Min.)}}{\text{Dye concentration (cc/Liter)}}$$

#### METHODS

##### *The Iodine Phantom (Fig. 1)*

A set of 10 plexiglass tubes (6.7 mm. internal diameter) are filled with solutions of Hypaque® of known concentrations ranging from 1 to 10 per cent. These tubes are mounted in a plexi-

\*This report was presented at the Staff Meeting of the University of Minnesota Hospitals on March 2, 1962.

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glass block  $1\frac{1}{2}$  inches thick. This "iodine phantom" is placed alongside the artery, and its radiograph is taken during the injection of contrast medium. The optical density of the opaque medium in the artery is compared with the density of the "iodine phantom," and the dilution is calculated from the attenuation factor curve.

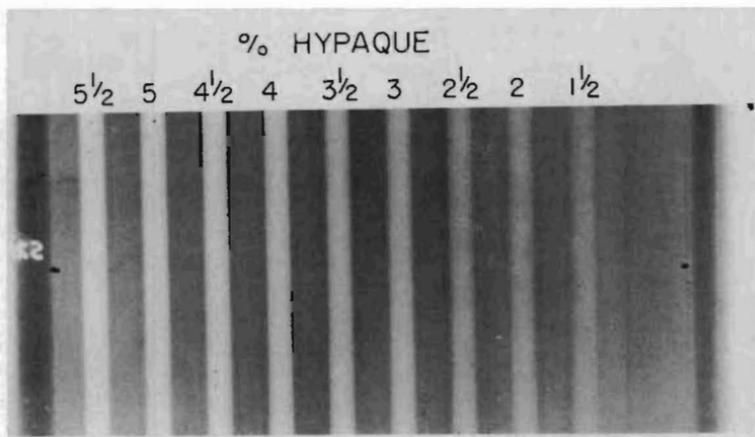


Fig. 1a

Radiogram of the "iodine phantom." The "Hypaque" concentrations in the various tubes are different from those mentioned in the text.

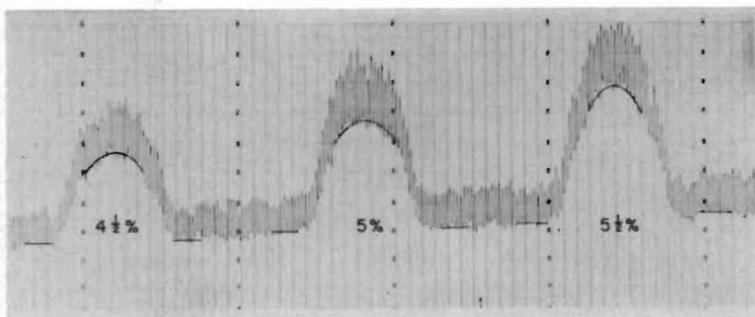


Fig. 1b

Densitometric recording of the radiogram. The difference in the density corresponding to a variation of  $\frac{1}{2}$  percent in the concentration of the "Hypaque" is easily measured.

*The Injection of the Indicator*

Fifty per cent Hypaque solution is preferred as the opaque indicator because it has the least effect on the blood flow, as will be shown later. Concentrations of Hypaque exceeding 50 per cent have specific gravities too high to permit satisfactory mixture with the blood stream and tend to "pool." The injection is carried out at a constant rate of 15 to 38 cc/minute with a Harvard constant withdrawal/infusion pump.

The opaque medium is delivered through a No. 90 polyethylene catheter with a sealed end and two fine side holes.

*The Flow Model*

Water containing a small amount of detergent is siphoned from two five-gallon containers (Fig. 2) through a polyvinyl tube. The detergent minimizes the formation of air bubbles in the system.

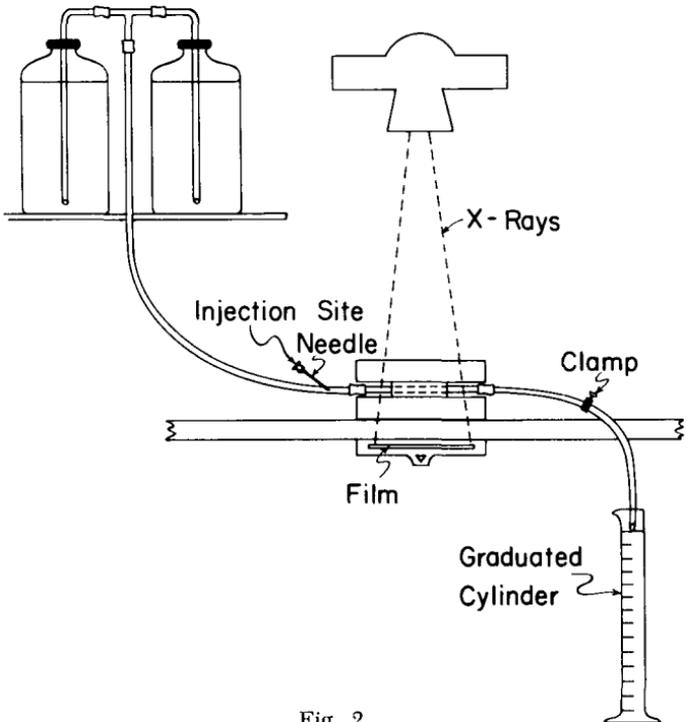


Fig. 2  
Diagram of the flow model

The water flows at a constant rate through a plexiglass block (12 cm. thick) which is placed on the radiographic table to serve as a radiographic phantom. From this phantom the water flows through a plastic tubing in a graduated cylinder. The rate of flow is controlled by an adjustable Hoffman clamp fitted on the distal end of the plastic tubing. The quantity of water collected in the cylinder in a period of one minute is a direct measurement of the flow rate.

The contrast material is injected upstream and very close to the plastic phantom through a No. 90 polyethylene catheter. In every experiment the flow rate was determined directly and radiographically. A radiograph of the flowing mixture of contrast material and water through the phantom is typically taken one second after the beginning of the injection.

#### *Femoral Artery Flows in the Dog*

Mongrel dogs weighing about fifteen kilograms are anesthetized with Surital.<sup>®</sup> The femoral artery is exposed, and an electromagnetic flow meter probe is placed around the femoral artery just distal to the inguinal ligament. A polyethylene catheter is introduced into the common femoral artery

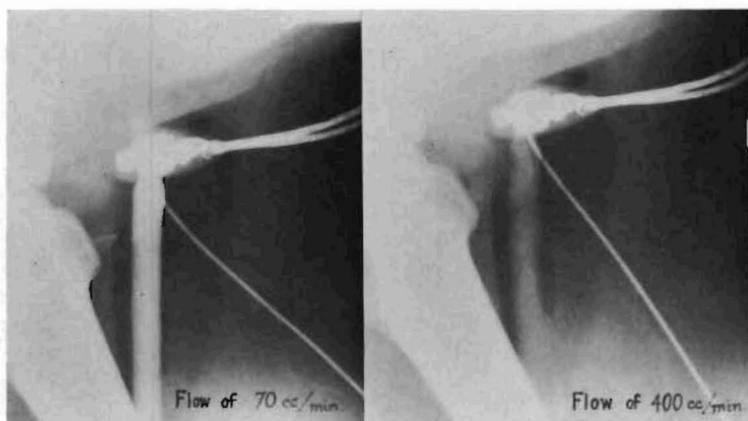


Fig. 3

Radiogram of the femoral artery in the dog. The probe of the electromagnetic flowmeter is seen just distal to the inguinal ligament. The polyethylene catheter through which the injection is performed is on the right side. The difference in the concentration of the "Hypaque" due to the difference in flow is obvious.

through one of its muscular branches. In its final position the tip of the catheter lies about two centimeters distal to the probe. All the branches of the femoral artery between the catheter tip and the probe are ligated.

A canula is introduced in the other femoral artery for continuous pressure recording. A simultaneous recording of the flow and the blood pressure are made just before the injection of Hypaque.

The dog is positioned so that the femoral artery lies parallel to the x-ray table. The previously described "iodine phantom" is placed alongside the artery (Fig. 3).

### *The Radiograph*

The exposure is made at 70 or 80 kilovolts, 10 to 15 milliamperes for a period of two seconds. A radiograph is taken one second after the beginning of the injection. The injection of the opaque medium is allowed to continue during the exposure and is discontinued immediately after.

Only Dupont films and Dupont par speed screens are used. The films are processed by the automatic developer. Stationary focused 12 to 1 grid with 110 line per inch is used, and the focal film distance is 40 inches.

### *The Densitometric Measurements*

A Bausch and Lomb microdensitometer with a light beam measuring 1/15 mm. in width and 0.75 or 1.0 mm. in length is used to scan the radiographs. The light transmission is recorded automatically on a Brown Recorder. The film is scanned at a speed of 4.4 mm/minute. Scanning is carried out perpendicular to the direction of the artery. This is followed by scanning of a standard plate of suitable density.

## MATHEMATICAL BASIS FOR CALCULATIONS

A. Determination of the gamma curve and preparation of the "standard plates."

Fifty-two Dupont films in cardboard holders are exposed to a diagnostic x-ray beam without a phantom at 30 kilovolts and 10 milliamperes. The exposure time is increased one second for every radiograph to cover a range from one to 52 seconds. All the films are developed in the automatic developer.

These films are scanned by the densitometer between two glass plates, with the light transmission through the center of the radiograph being taken as representative for that particular exposure. The amount of light transmission is converted into density by the following formula:

$$\text{Density} = -\log. \% \text{ transmission.}$$

The densities and the relative exposures from one to 52 seconds are plotted on regular graph paper as in Figure 4. The resulting plot is the gamma curve of the photographic emulsion, the formula of which is:

$$D = 2.9102133 (1 - e^{-0.01493125 E}),$$

where D = Density and E = Relative energy of exposure.

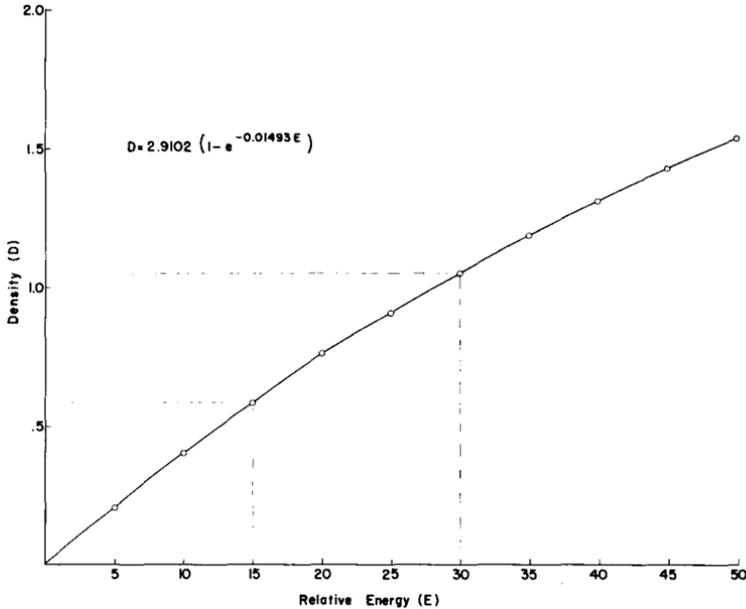


Fig. 4

Graph representing the increase of the optical density of the Dupont film with the increase of the relative energy (i.e. relative exposure) deposited in the photographic emulsion. The optical density of the base of the film is considered zero. If the density of the artery is 0.584 and the density of the background is 1.05, the relative energy would then be 15 and 30 respectively. The x-ray beam has thus been attenuated to half its original intensity, and the attenuation factor in this case is 0.5.

The density of the unexposed and unfogged film is considered to be zero. The gamma curve is independent of the quality of the radiographic beam and is constant for the same

type of photographic emulsion as long as the developing process is constant.<sup>10-12</sup> Six representative radiographs are selected from the exposed 52 films and mounted between two glass plates. These are "standard plates," the density of which is the reference point for the density of the radiograph of the artery in question.

B. Attenuation Factor

The attenuation factor represents the attenuation of the x-ray beam by contrast medium present in the injected artery. Since the artery is imbedded in soft tissues there is also at-

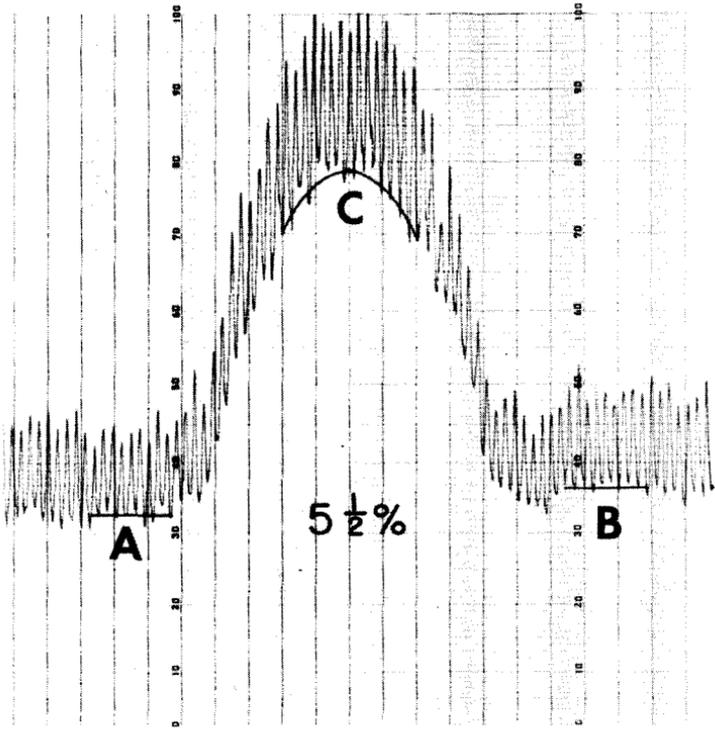


Fig. 5a

Densitometric recording of one "iodine phantom" tube. The average density in A and B represents the background density and the density at the peak C represents the density of the artery. The attenuation factor is calculated from the ratio of the corresponding relative energies.

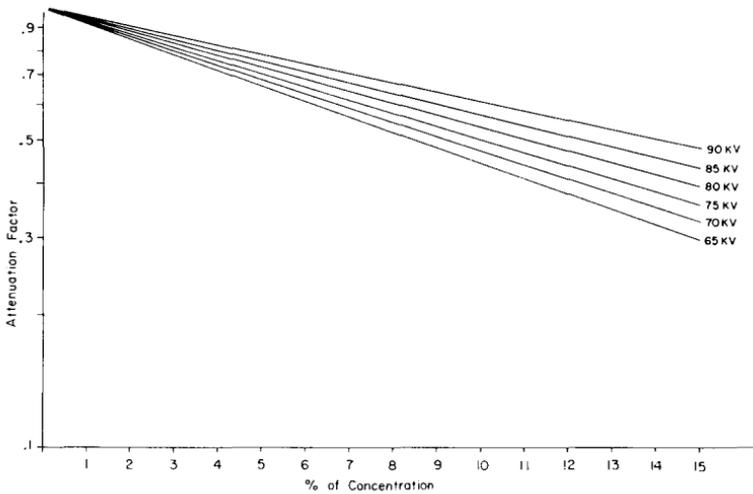


Fig. 5b

Graph representing the variation of the attenuation factor with the percent concentration of "Hypaque" and the kilovoltage.

tenuation of the x-ray beam by soft tissue structures. The actual attenuation factor therefore is the ratio between soft tissue and artery density. If the intensity of the x-ray beam after its passage through soft tissue is called X and the intensity after its passage through the artery is called Y, the ratio X over Y represents the attenuation factor. This relationship is constant regardless of changing magnification and changing milliamperere seconds.

By plotting attenuation factor against the percentage concentration of Hypaque on a semi-log scale, one obtains a straight line, as in Figure 5b. The slope of this line changes with the number of kilovolts and is also affected by the thickness of the part examined. Secondary scattered radiation increases with the thickness of the part examined and consequently tends to diminish the contrast between artery and soft tissue, thus diminishing the slope of the attenuation factor curve. To compensate for this factor the "iodine phantom" is radiographed together with the examined part.

The attenuation factor of three phantom tubes is determined, and their values are plotted on semi-log paper against the known concentration of Hypaque in these tubes. A straight line

drawn through these points obviously intersects the ordinate axis at 1.0 (Fig. 6). The attenuation factor of the artery injected with contrast medium is determined from the densitometric recording, and the corresponding Hypaque concentration in the artery is obtained from this graph.

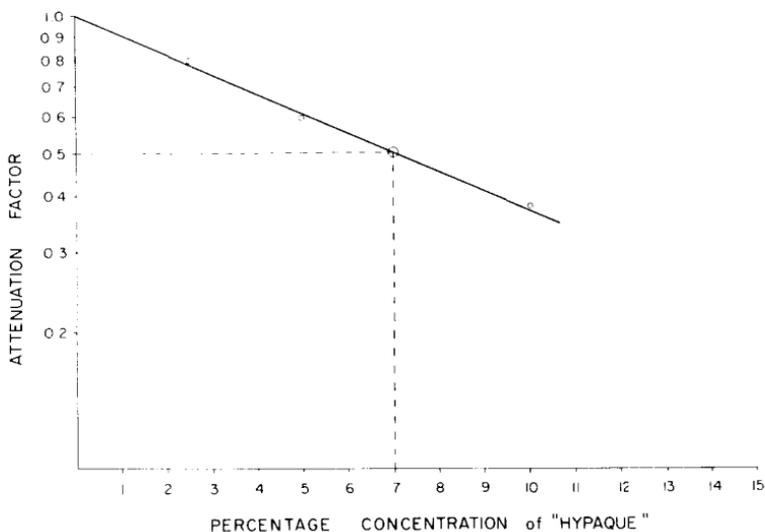


Fig. 6

Determination in per cent of the concentration of "Hypaque" in the artery. In this case the artery has attenuated the beam to half its original value, and the corresponding concentration is 7%. The other three points on the graph are those of tubes of known concentration in the "iodine phantom" the radiograph of which is taken with the artery.

### C. Correction for the size of the Artery

The diameter of the artery can be measured directly on the radiograph or from the densitometric recording.

The actual concentration of the Hypaque in the artery is determined by:

$$\frac{c \times T}{A} = C,$$

where:  $c$  = concentration of the Hypaque computed in step B,  
 $T$  = inside diameter of tube in iodine phantom,  
 $A$  = diameter of the artery,  
 $C$  = actual Hypaque concentration in the artery.

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TABLE 1  
LARGE TUBE EXPERIMENTS (6.7 MM I.D.)  
IODINE PHANTOM

Experiment No.	Actual Flow cc/Min.	Flow by Radiography cc/Min.	Percentage Error
1	469	501	+ 6.8 %
2	467	479	+ 2.56%
3	183	176	- 4.0 %
4	181	174	- 3.8 %
5	292	283	- 3.0 %
6	357	369	+ 3.3 %
7	352	339	- 3.7 %
8	347	321	- 7.5 %
9	86	91	+ 5.8 %

TABLE 2  
SMALL TUBE EXPERIMENTS (3.3 MM I.D.)  
FLOW MODEL STUDIES

Experiment No.	Actual Flow cc/Min.	Flow by Radiography cc/Min.	Percentage Error
10	450	453	+ .6%
11	448	453	+ 1.1%
12	245	244	- .5%
13	244	261	+ 6.9%
14	144	145	- .6%
15	45	46	- 2.2%
16	68	63.5	- 3.5%
17	68	71	+ 4.4%
18	105	115	+ 9.5%
19	260	267	+ 2.7%
20	443	426	- 3.9%
21	441	431	- 2.3%
22	247	247	0 %
23	244	243	- 0.4%
24	70	72	+ 2.8%
25	68	69	+ 1.5%
26	68	72	+ 5.8%

D. The flow is calculated from the Hamilton-Stewart Formula as follows:

$$\text{Flow (cc/Min.)} = \frac{\text{Injection rate (cc/Min.)} \times \text{Concentration of Hypaque injected}}{\text{Concentration of Hypaque in artery}}$$

## RESULTS

Many flow determination experiments were performed with the flow model using different size plexiglass tubes. The results are summarized in Tables 1 and 2. The results of the experiments on femoral artery flow in the dog are listed in Table 3. The error is measured as the percentage variation of the radiographic technique from the direct measurement or the electromagnetic flowmeter recording.

TABLE 3  
FEMORAL ARTERIAL FLOW IN THE DOG

Experiment No.	Flow by Electromagnetic Flow Meter cc/Min.	Flow by Radiography cc/Min.	Percentage Error
1	80	88	+ 9.1%
2	120	111	- 8.1%
3	108	102	- 5.5%
4	401	352	- 12.2%
5	76	87	+ 12.7%
6	75	78	+ 4.0%
7	79	85	+ 7.5%
8	82	80	- 2.5%
9	73	80	+ 9.5%

## DISCUSSION

*Effect of Injecting Contrast Material*

In the experimental animal the injection of the 50 per cent Hypaque sometimes causes a minor initial decrease in the flow starting three seconds after the injection and continues until the tenth second after the injection. This decrease in flow is also observed in the model and is apparently due to the viscosity of the contrast medium. This is followed by a sudden sharp increase in the rate of flow to about three times its original value within 35 seconds from the beginning of the injection. The return to the original rate of flow is slow and gradual over a

period of one and one-half to two minutes. Because of this effect on the flow the exposure is taken one to two seconds after the injection. Figure 7 shows the effect of injecting a 75 per cent solution of Hypaque on the femoral arterial flow in a dog as determined by the magnetic flowmeter. The comparative effect of various contrast media is shown in Figure 8.

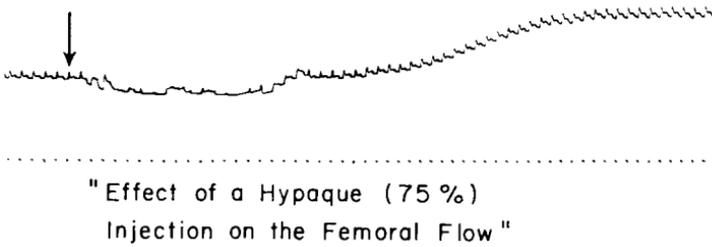


Fig. 7

Electromagnetic recording of the femoral arterial flow in the dog after the injection of 75% "Hypaque." There is an initial decrease followed by an increase in the flow.

#### *The Injection Catheter*

As previously noted, Hypaque is injected in the artery through a polyethylene catheter No. 90 having 2 fine side holes and a sealed end. Two jets of opaque medium are thus formed, causing enough turbulence in the flow to prevent streaming of the relatively dense Hypaque solution in the most depending part of the artery. High speed motion-picture study in the flow model revealed no evidence of streaming close to the injection site.

#### *The Radiographic Sampling*

In their excellent review of the subject of the sampling error in the standard Fick and dye methods, Visscher and Johnson,<sup>13</sup> Stow,<sup>14</sup> Rossi et al.,<sup>15</sup> and Fox and Wood<sup>16</sup> have recommended the approximation of the injection and sampling sites and the avoidance of sampling from a branch of the main stream.

The concentration of the contrast material by the radiographic technique is determined at a point very close to the injection site where enough turbulence is induced by the injection itself. One of the major advantages of this method is that it obviates the need for direct sampling. With all sampling techniques, complete mixing is absolutely necessary, and the indicator must be injected far proximal to the sampling site.

The flow in a single artery can therefore only be measured with difficulty. In spite of incomplete mixing, radiographic density of the artery will, however, be the same as in the case of actual complete dissolution of the indicator.

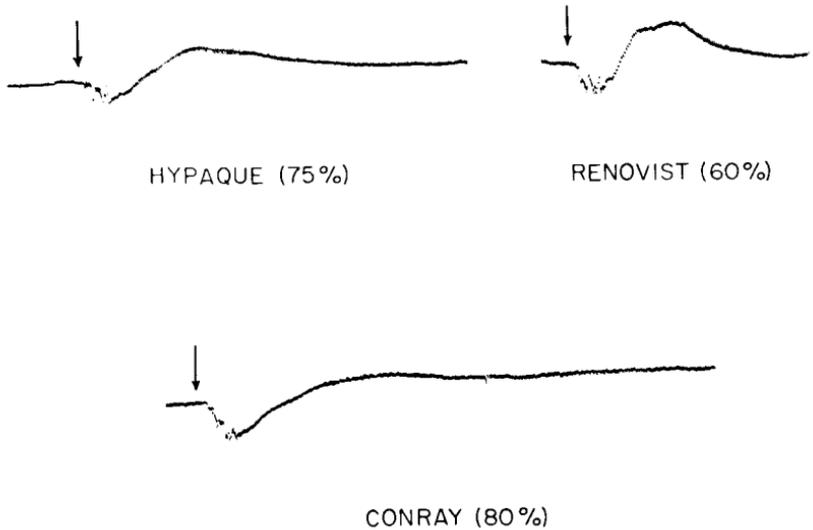


Fig. 8

Comparative effect of various contrast media on the femoral arterial flow in the dog. "Hypaque" has the least effect and the recovery is fast.

#### *The Recirculation of the Indicator*

Since the radiograph of the artery is made within two seconds after injection is begun, no recirculation can be detected. In two experiments in which four consecutive injections a few minutes apart were made in the femoral artery of the dog, the values of the flow rate were not altered by the recirculating opaque medium. The added opacity is not enough to be detected, thus offering another advantage over standard dye dilution techniques.

#### CONCLUSION

A radiographic contrast dilution technique was developed and tested in flow models and animals. The high accuracy of the obtained results is encouraging. The technique offers several advantages over standard indicator dilution methods:

- 1) It is easily performed during angiographic procedures.
- 2) Sampling with a needle or a catheter distal to the injection site is not necessary.
- 3) Recording of a time-concentration curve is not necessary, since recirculation is not detectable.

Currently under investigation is the practical application of this technique for determination of carotid femoral and renal blood flow in human subjects. Its value for determination of cardiac output and measurement of right to left and left to right shunts is being contemplated.

*Acknowledgments:* The authors are grateful to J. Longerbeam, M.D., and Richard Lillehei, M.D., Ph.D., for their advice and help in the electromagnetic flow meter measurements.

Mr. Edgar R. F. Winter, Ph.D., from the department of Mechanical Engineering has been of great help in providing the densitometer and advice on using it.

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## Staff Meeting Report

### The Treatment of Experimental Acute Hemorrhagic Hypotension with Mixtures of Pressor Amines\*

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Raymond N. Bieter, M.D., Ph.D.‡

The use of pressor agents to correct hypotensive states is based on the premise that they can halt or prevent the progression to the shock state. This premise is not agreed upon by all clinicians, nor is it unanimously supported by research evidence.

According to the literature, the use of pressor agents in clinical and experimental hypotensive and shock states has not been rewarding. Studies have shown that a high percentage of the subjects exhibit a favorable initial pressor response, but the ultimate survival rate is less than 40 per cent.<sup>1-3</sup> It is now held that death is due to a prolonged deficiency of blood flow to the tissues which causes the evolution of a cyclic, self-perpetuating process resulting from the interaction of peripheral vascular failure and disruption of tissue homeostatic mechanisms.<sup>4-6</sup>



John D. Palmer

Opposition to the use of pressor agents stems from the belief that they may augment the vasoconstrictive phase of shock and further embarrass capillary flow.<sup>7-9</sup> In the balance is the question of whether or not the increase in arterial pressure is sufficient to offset the increased resistance and thus appreciably increase flow in the microcirculation. Present clinical and experimental evidence does little to resolve this question.

The unfavorable results obtained with the clinical and experimental use of the pressor drugs point up the need for a new approach to the treatment of hypotensive states. According-

\*This report was presented at the Staff Meeting of the University of Minnesota Hospitals on January 19, 1962.

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‡Professor and Head, Department of Pharmacology, University of Minnesota

ly, we decided to attempt a solution to this problem by using mixtures of pressor agents.

## METHOD

Adult mongrel dogs anesthetized with 30 mg/Kg pentobarbital were subjected to massive hemorrhage via a catheter placed through a femoral artery into the abdominal aorta. Bleeding was allowed to continue until a volume of blood equivalent to 5 per cent of the body weight had been lost. If respiratory or cardiac arrest or both appeared imminent, or if the flow of blood diminished to a slow drip, the hemorrhage was terminated and the infusion therapy was begun. Arterial blood pressure was followed with a Sanborn Electromanometer and, along with the Lead I electrocardiogram, was recorded on a Sanborn Twin-Viso recorder. Pulse wave and electrocardiographic patterns were observed directly on an oscilloscope.

Upon completion of the hemorrhage, a course of intravenous infusion therapy was instituted. Groups of 10 dogs received one of the forms of treatment shown in Table 1. The rate of administration, dosage, and duration of infusion were determined by the response of the animal. Blood pressure, pulse, respiration, and electrocardiogram were monitored at 15 minute intervals for a period of four hours. The pilot studies demonstrated that therapy beyond 75 minutes yielded no further benefit. Thus at 75 minutes following hemorrhage, therapy was discontinued regardless of the condition of the animal. The animals surviving at the four hour mark were returned to the kennel. Animals surviving for 24 hours after the hemorrhage were considered permanent survivors.

TABLE 1  
PRESSOR AGENTS EMPLOYED

Drugs*	Ratio	Concentration μg/L
Saline Solution	—	—
Phenylephrine	—	8000
Norepinephrine	—	800
Phenylephrine/Norepinephrine	5:1	2000:400
Phenylephrine/Norepinephrine	7.5:1	3000:400
Phenylephrine/Norepinephrine	10:1	4000:400
Phenylephrine/Norepinephrine	15:1	6000:400
Phenylephrine/Norepinephrine	20:1	8000:400

\*Doses of 1-norepinephrine calculated as free base. Doses of phenylephrine calculated as HCl salt. Solutions were made in 0.9% saline.

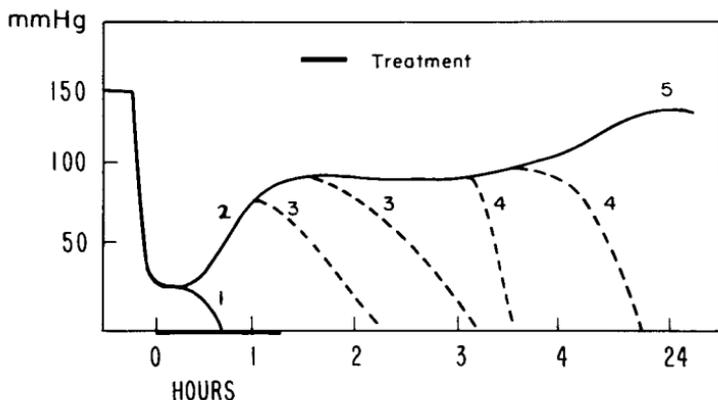


Fig. 1

Systolic Arterial Pressure Trends Following Massive Hemorrhage with Subsequent Infusion Therapy, Drawn after Wiggers

#### RESULTS

The response to the hemorrhage and subsequent therapy is represented in a generalized fashion in Figure 1. One can note that blood pressure fell precipitously with the letting of the blood; then, with the institution of therapy, one of several trends developed: (1) lack of response with rapid progression to death; (2) initial recovery followed by (3) gradual circulatory failure and death; (4) sudden death after apparent good recovery; (5) continued recovery. Examples of each of these trends occurred in every group except the 10:1 treated series, in which all of the animals went on to permanent survival. Table 2 shows the number of survivors in each group. Figures 2 through 5 are representative composites of the blood pressures for the four hour post-hemorrhage period. Each point on the curve represents the mean diastolic or systolic pressure for the entire group of ten animals. Thus even though a given animal had died, its pressure 0/0 was used in the calculation. Each figure also has an indication of the mean duration of treatment. In general each animal was treated according to its apparent needs. Thus those who responded promptly and favorably usually received smaller doses of drug and shorter periods of therapy than those who did not respond as well.

The fortuitous decision to study first the 10:1 mixture led to the formulation of the treatment format for the remainder of the study. The first three animals given this mixture exhibited prompt and favorable responses to small doses of the mixture

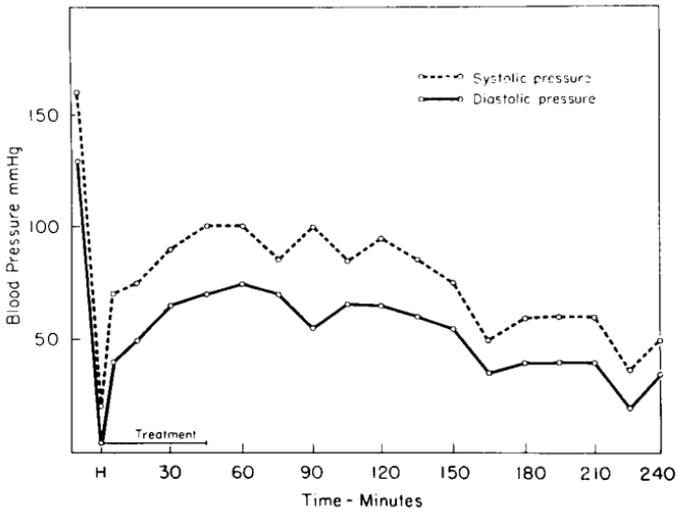


Fig. 2  
Results of Treatment with Saline Solution

given over a short period of time (not in excess of 75 minutes). These animals were killed four hours following the hemorrhage and were observed to exhibit no gross or microscopic tissue changes. Since this was believed to be an optimal response which could serve as a basis for comparison, the duration of treatment and volume of fluid administered to the other groups were held to comparable levels.

TABLE 2  
SURVIVALS FOLLOWING TREATMENT

Treatment	Survivors
Saline Solution	3/10
Phenylephrine	4/10
Norepinephrine	4/10
Phenylephrine/Norepinephrine 5:1	3/10
Phenylephrine/Norepinephrine 7.5:1	3/10
Phenylephrine/Norepinephrine 10:1	10/10
Phenylephrine/Norepinephrine 15:1	4/10
Phenylephrine/Norepinephrine 20:1	3/10

The animals receiving saline solution, norepinephrine, or phenylephrine followed essentially the same course. A prompt rise in blood pressure stabilized in 45 minutes at approximately 100/75. In the cases of the phenylephrine and norepinephrine therapies the pressure began to decline gradually after 65 minutes, and with the saline solution treatment the pressure began to fall at the 120 minute mark. The blood pressure of the groups treated with phenylephrine-norepinephrine mixture followed essentially the same course. But the magnitude of the pressor response and the length of time before the blood pressure began to decline were less than those observed in the three groups just mentioned. The one exception occurred among the group treated with the 10:1 mixture. In these animals the blood pressure rose sharply with the institution of therapy and continued to rise even after the discontinuance of the infusion. These animals were noted to be normotensive four hours after hemorrhage induction.

TABLE 3  
COMPARISON OF DRUG THERAPY TO SALINE SOLUTION THERAPY

Therapy	Hemorrhage <sup>a</sup> % Body Weight		Bleeding Time <sup>a</sup> Minutes		Volume of Infusion <sup>a</sup> cc/kg	
	$\bar{X}$	P	$\bar{X}$	P	$\bar{X}$	P
Saline solution	4.6	-	7.0	-	12.7	-
Norepinephrine	4.9	< 0.05	6.5	> 0.05	10.8	> 0.05
Phenylephrine	4.6	> 0.05	6.2	> 0.05	12.5	> 0.05
Phenylephrine/Norepinephrine mixtures						
5:1	4.9	< 0.05	6.6	> 0.05	9.8	> 0.05
7.5:1	4.5	> 0.05	6.9	> 0.05	8.6	< 0.05
10:1	4.7	> 0.05	4.7	< 0.05	12.4	> 0.05
15:1	4.7	> 0.05	6.1	> 0.05	9.0	> 0.05
20:1	4.8	> 0.05	8.2	> 0.05	8.5	< 0.05

<sup>a</sup> $\bar{X}$  = Mean    P = Significance

Table 3 represents a summary and analysis of the treatment. In order to evaluate the treatment satisfactorily, the variables of bleeding time, bleeding volume, and volume of fluid administered were compared statistically for each of the groups treated with drugs and for the group treated with saline solution. When tests revealed a significantly greater number of survivors in the 10:1 treated group, a similar comparison was performed and

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this is shown in Table 4. Table 5 shows the mean dosage, in micrograms/Kilogram body weight for each of the eight treatment groups.

TABLE 4  
COMPARISON OF ALL OTHER FORMS OF THERAPY  
TO THE 10:1 MIXTURE THERAPY

Therapy	Hemorrhage <sup>o</sup>		Bleeding Time <sup>o</sup>		Volume of Infusion <sup>o</sup>	
	% Body Weight		Minutes		cc/Kg	
	X	P	X	P	X	P
Phenylephrine/Norepinephrine mixtures						
10:1	4.7	-	4.7	-	12.4	-
5:1	4.9	> 0.05	6.6	< 0.05	9.8	> 0.05
7.5:1	4.5	> 0.05	6.9	< 0.05	8.6	> 0.05
15:1	4.7	> 0.05	6.1	> 0.05	9.0	> 0.05
20:1	4.8	> 0.05	8.2	< 0.05	8.5	> 0.05
Saline solution	4.6	> 0.05	7.0	< 0.05	12.7	> 0.05
Norepinephrine	4.9	> 0.05	6.5	< 0.05	10.8	> 0.05
Phenylephrine	4.6	> 0.05	6.2	< 0.05	12.5	> 0.05

<sup>o</sup>X = Mean    P = Significance

TABLE 5  
TOTAL DOSAGE OF PRESSOR AGENTS ADMINISTERED

Therapy	Dose <sup>o</sup> μg/Kg
Saline Solution	—
Phenylephrine	100
Norepinephrine	8.7
Phenylephrine/Norepinephrine Mixtures	
5:1	{ PE 19.5 NE 3.9
7.5:1	{ PE 27.0 NE 3.4
10:1	{ PE 50.0 NE 5.0
15:1	{ PE 54.0 NE 3.6
20:1	{ PE 70.0 NE 3.4

<sup>o</sup>PE = Phenylephrine HCl    NE = Norepinephrine as free base

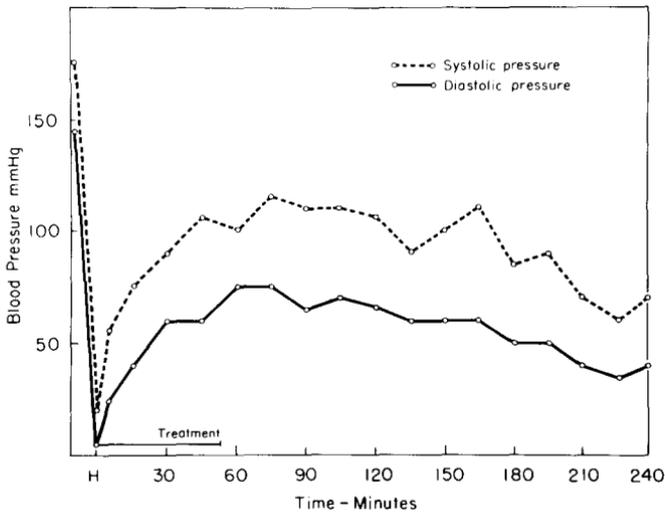


Fig. 3  
Treatment with Norepinephrine

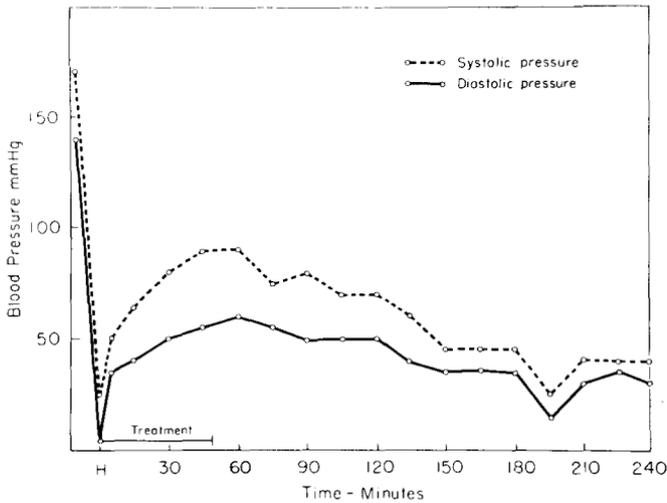


Fig. 4  
Treatment with Phenylephrine and Norepinephrine, 5:1

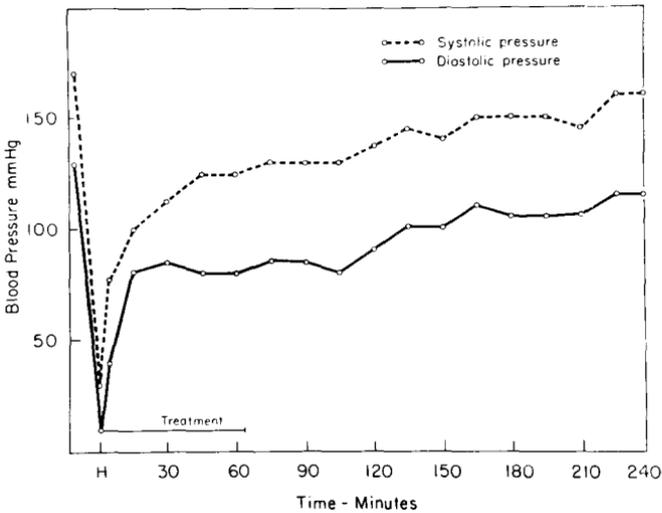


Fig. 5

Treatment with Phenylephrine and Norepinephrine, 10:1

#### DISCUSSION

Induced acute hemorrhage in the dog was used to study the efficacy of pressor amine mixtures in the treatment of acute hemorrhagic hypotension (latent hemorrhagic shock). The experimental technique used did not possess the ease of reproducibility of the Lamson<sup>10</sup> or Lillehei<sup>7</sup> methods, but nevertheless, a fair degree of uniformity was achieved. The purpose of inducing hemorrhage was to lower blood volume to a level which would lead to death via hemorrhagic shock. The statistical comparison of the data concerning bleeding volume, bleeding time, and volume of infusion for each drug treated group to that of the saline and 10:1 treated groups was necessary to determine if there was a valid basis for the evaluation of the therapy.

Wiggers, in a survey of the literature from 1915 to 1945, found that lethal canine bleeding volumes ranged from 3.7 to 8.8 per cent of body weight.<sup>11</sup> In a series of 195 dogs studied in his laboratories, irreversible shock was produced by the withdrawal of blood volumes equivalent to 3.0 to 5.5 per cent of body weight, with the greatest number falling between 4.0 to 5.0 per cent. The mean bleeding volumes for this study fall well within this range. The 5:1 and norepinephrine treated animals lost slightly more blood on the average than did the group

treated with saline solution, but no group differed significantly from the 10:1 group.

With respect to bleeding time, only that of the 10:1 group was shorter than that of the control group (saline solution). Bleeding times for all except the 15:1 group were significantly longer than for the 10:1 groups. But since Wiggers and Price have concluded that the effects of acute hemorrhage are much the same whether the blood is let rapidly or slowly, continuously or intermittently, no great significance was ascribed to the differences in bleeding times.<sup>11,12</sup>

The volume of fluid returned to the animals ranged on the average between 0.85 and 1.3 per cent of their body weights. The 5:1 and 7.5:1 groups received significantly less fluid than did the control animals, but none of the groups differed from the 10:1 group. The 30 per cent survival rate observed in the control group served as a baseline for the evaluation of the drug therapy.

The course of events following treatment with saline solution, phenylephrine, norepinephrine, and the mixtures phenylephrine-norepinephrine (except the 10:1 mixture) was similar to that observed in the clinical usage of the agents.<sup>1,2</sup> Initially, blood pressure responded favorably in most of the animals, but in the final analysis 40 per cent or less survived in each group. This result demonstrates the inadequacy of the pressor agents in the treatment of hemorrhagic hypotension. It further emphasizes that blood pressure *per se* is an inadequate criterion in assaying shock state and that an adequate pressor response is not synonymous with alteration of the basic mechanisms which lead to irreversible shock.

The animals treated with the 10:1 mixture had initial pressor responses which were similar to those observed in the other seven groups, but their blood pressure levels continued to rise while the rate of drug infusion was being reduced and after cessation of therapy. Similar patterns of response rarely occurred in the other seven groups. In these groups some animals followed a similar course but died less than 24 hours after hemorrhage. This finding may indicate a different mechanism of action for the 10:1 mixture.

The initial increase in blood pressure can be ascribed to the normal physiologic response to massive hemorrhage, i.e., a generalized vasoconstriction, and secondarily to volume replacement, though this was minimal.<sup>13</sup> This assumption is supported by the fact that the animals treated with saline solution responded similarly to those treated with drugs. Only therapy with the 10:1 mixture proved adequate. It is not certain why this form of

treatment—and more specifically this particular mixture ratio—should be superior to others.

Susceptibility may be determined by the level of function of the cardiovascular homeostatic mechanisms. The ability of the animal to maintain a high level of function of these mechanisms—either with or without the benefit of therapy—thus determines the state of susceptibility.<sup>4</sup> Since the 10:1 mixture of phenylephrine and norepinephrine effected survival in all of the animals in which it was used, this mixture ratio clearly must have prevented the physiologic changes which induce or perpetuate shock syndrome. As shock is presently understood, this would mean that: 1) adequate blood flow was maintained to the organs essential for immediate survival; and 2) blood flow to the less vital areas (i.e., areas where inadequate flow is thought to bring about the changes which cause, perpetuate, or accelerate shock) was not diminished below critical levels.<sup>4,5</sup>

From the known pharmacologic properties of these agents we can surmise that the 10:1 ratio brought about an increased vasomotion with diminution of capillary filling, increased reabsorption of interstitial fluid, increased circulating blood volume, and increased venous return.<sup>5</sup> Furthermore, cardiac performance may have improved as a result of increased coronary flow and direct myocardial stimulation.<sup>14,17</sup> All these factors suggest that either increased cardiac output or increased peripheral resistance or both may have caused the sustained blood pressure response in these animals.

The doses of pressors given to these animals were minute. When it became apparent that the 10:1 mixture was highly effective in small doses, we decided to limit the dosage of the other forms of therapy to comparable levels. Clinically doses of norepinephrine from 1.5 to 25 microgram/Kilogram/minute in amounts of 40 to 80 mg. per day have been used.<sup>18,19</sup> Keys<sup>20,21</sup> has maintained that a dose of 0.05 mg/Kg of phenylephrine is effective, and 1.5 mg. is the maximum safe dose. These doses are many times greater than those used in this study. Parkins et al.<sup>22</sup> observed optimum results in treating canine hemorrhagic shock with volumes of saline solution equivalent to 8 to 12 per cent of body weight—i.e., six to nine times greater than the volumes used in our study.

Lacking definitive hemodynamic evidence, one can only speculate about the mechanism of action of the 10:1 mixture—e.g., the mixture may have altered vessel reactivity, caused the release of endogenous norepinephrine, prevented the binding of circulating norepinephrine, or altered the metabolism of endogenous norepinephrine.<sup>23-25</sup>

## SUMMARY

Experimentally induced acute hemorrhagic hypotension was used in dogs to study the efficacy of treatment with mixtures of phenylephrine and norepinephrine. Survival following treatment with saline solution and with each drug given independently did not exceed 40 per cent. Similar survival rates were experienced utilizing the phenylephrine-norepinephrine mixture therapy except in the group receiving the 10:1 mixture, in which there was 100 per cent survival.

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# Medical School News

## MEDICAL SCHOOL REPORTS

### RISE IN STUDENT APPLICATIONS

The University of Minnesota Medical School has experienced a 30 percent increase during the past year in the number of student applications for admission.

A total of 504 students—largest group in ten years—applied for places in the 1962 Freshman Class, and 150 have been admitted, Dr. Robert B. Howard, Dean of the Medical Sciences, announced. They will comprise the largest class in the Medical School's history.



Robert B. Howard

Last year 392 students applied for the 140 places available. In 1960, 337 applied, and in 1959, 319 sought admittance. The rise in the number of applicants is an encouraging sign, Dr. Howard said, that medicine as a career may again attract many of the top quality students who graduate each year from the nation's colleges and universities.

Applications are apparently on the upswing again nationally, according to the Association of American Medical Colleges.

One thousand more applicants are expected this year at U.S. Medical Schools. The peak year for applicants was 1948, the "veterans boom year," when 25,000 students sought admittance in the 6,600 freshman places offered at medical schools. They represented 9 per cent of all the college graduates of that year. The downtrend hit bottom in the early 1950s then stabilized. In 1961, about 15,000 students competed for 8,500 places available in 85 medical schools, but they represented only 4 per cent of the year's college graduates.

Minnesota's surge in applications has been accompanied by an improvement in quality of applicants, believes Dr. William Fleeson, Assistant Dean. "We think today's best students are the equal of any of their predecessors, and we are convinced that the lower 20 to 30 percent of today's classes are stronger academically than those of recent years.

A larger pool of college students, closer attention by doctors and alumni, and an improved financial picture are likely reasons for Minnesota's increase, he said.

Scholarship funds of about \$40,000 are available at the Medical School this year, strengthening the School's competitive position with other state and private medical schools. The Minnesota Medical Foundation's scholarship aid program is one of the most significant factors in the rise, he said. The Foundation, a privately endowed organization of doctors and laymen, annually supplies about fifty scholarships worth \$500.00 each to Medical School students.

The Medical School has traditionally trained and supplied most of the state's physicians. An estimated 2,400 of Minnesota's 3,800 practicing physicians are graduates of the institution, and the vast majority of 6,000 doctors who have received medical degrees from Minnesota in the past 75 years were residents of the state when they enrolled. Others who train at University of Minnesota have been residents of neighboring states, particularly the Dakotas and Montana. The 1962 Freshman class of 150 members will include 16 who are non-residents of Minnesota.

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### **MEDICAL SCHOOL RECEIVES \$17,101.32 FROM 1961 A.M.E.F. CAMPAIGN**

The University of Minnesota Medical School received \$17,101.32 as its share of funds contributed to the American Medical Education Foundation during 1961. More than \$1.3 million was contributed by physicians during the year to the A.M.A.-sponsored program.

Approximately one-third of the total was undesignated to any medical school. Minnesota received \$4,236.07 from the undesignated pool. Physicians earmarked an additional \$12,865.25 to the aid of the Medical School.

Dr. Robert B. Howard, Dean of the College of Medical Sciences, thanked contributors who aided the program, calling their gifts "among the most valuable we receive because of the lack of restriction as to their use."

He said the Medical School has used the funds, for example, to help replace and modernize teaching equipment in the basic science departments; to support temporary instructorships and lectureships in both basic and clinical departments; and to provide special equipment needs of the University's new Diehl Hall bio-medical library.

**INTERNSHIPS ANNOUNCED FOR CLASS OF 1962**

Internship assignments have been announced for the 118 members of the 1962 graduating class, University of Minnesota Medical School.

Forty-nine graduates will remain in Minnesota and intern at eight different hospitals. Nine will be at Minneapolis General Hospital, eight at Bethesda Hospital, St. Paul, and seven at the University of Minnesota Hospitals.

Thirty graduates will intern at 10 hospitals in California, as usual, the second most popular state for an internship location. The remainder were matched to hospitals in 13 other states.

The Class of 1962 and appointments:

- |   |  |
|---|--|
| ABRAMSON, MICHAEL B.<br>Southern Pacific General Hosp.<br>San Francisco, Calif. | BINET, EUGENE F.<br>St. Mary's Hospital<br>Minneapolis, Minnesota              |
| ALEXANDER, DAVID G.<br>St. Mary's Hospital<br>Minneapolis, Minnesota            | BORNFLETH, LESLIE R.<br>Brackenridge Hospital<br>Austin, Texas                 |
| ALEXANDER, HARLAN G.<br>Children's Memorial Hospital<br>Chicago, Illinois       | BRANCH, KENNETH A.<br>General Hospital of Riverside<br>Arlington, California   |
| ANDERSON, C. ARTHUR<br>Santa Clara County Hospital<br>San Jose, California      | BRENDE, JOEL O.<br>Bethesda Hospital<br>St. Paul, Minnesota                    |
| ANDERSON, QUENTIN N.<br>Philadelphia General Hospital<br>Philadelphia, Pa.      | BROWN, DAVID C.<br>Minneapolis General Hospital<br>Minneapolis, Minnesota      |
| ANSELMET, LOIS A.<br>St. Mary's Hospital<br>Minneapolis, Minnesota              | BURNES, KEITH C.<br>Naval Hospitals<br>Bethesda, Maryland                      |
| ANTOLAK, STANLEY J.<br>Philadelphia General Hospital<br>Philadelphia, Pa.       | BYCE, KENNETH R.<br>Milwaukee Hospital<br>Milwaukee, Wisconsin                 |
| ARNY, FREDERICK D.<br>Santa Clara County Hospital<br>San Jose, California       | CAMPION, BRIAN C.<br>St. Mary's Hospital<br>Duluth, Minnesota                  |
| BAKER, DANIEL R.<br>Minneapolis General Hospital<br>Minneapolis, Minnesota      | CLOUTIER, JOAN E.<br>Georgetown University<br>Washington, D.C.                 |
| BAKER, ROBERT M., JR.<br>Santa Clara County Hospital<br>San Jose, California    | CONLON, DANIEL C.<br>San Bernardino County Hosp.<br>San Bernardino, California |
| BALLHAGEN, JAY T.<br>Sioux Valley Hospital<br>Sioux Falls, South Dakota         | COWAN, GARY A.<br>St. Mary's Hospital<br>Duluth, Minnesota                     |
| BAYLEY, BRUCE C.<br>Cook County Hospital<br>Chicago, Illinois                   | CROWLEY, THOMAS J.<br>Charity Hospital<br>New Orleans, Louisiana               |
| BECCHETTI, JOHN J.<br>San Bernardino County Hosp.<br>San Bernardino, California | CULLIGAN, DAVID E.<br>Milwaukee County Hospital<br>Milwaukee, Wisconsin        |
| BENSON, VERNON R.<br>Bethesda Hospital<br>St. Paul, Minnesota                   | DAHLSTROM, DONALD D.<br>St. Mary's Hospital<br>Minneapolis, Minnesota          |
| BILSTAD, JAMES M.<br>Parkland Memorial Hospital<br>Dallas, Texas                | DEINARD, AMOS S.<br>Univ. of Minnesota Hospitals<br>Minneapolis, Minnesota     |
| BILTZ, JOHN F.<br>Gorgas Hospital<br>Canal Zone                                 | DIETZMAN, RONALD H.<br>Univ. of Minnesota Hospitals<br>Minneapolis, Minnesota  |

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- DRAGE, CHARLES W.  
Univ. of Minnesota Hospitals  
Minneapolis, Minnesota
- ECKERT, ROSEMARIE C.  
St. Mary's Hospital  
Minneapolis, Minnesota
- ELLINGSON, FREDERICK T.  
San Bernardino County Hosp.  
San Bernardino, California
- EMOND, JOSEPH S., JR.  
St. Mary's Hospital  
Minneapolis, Minnesota
- ENGSTROM, PAUL F.  
Univ. of Minnesota Hospitals  
Minneapolis, Minnesota
- ERICKSON, DONALD L.  
Baylor University Hospital  
Houston, Texas
- ERICKSON, WILLIAM D.  
Minneapolis General Hospital  
Minneapolis, Minnesota
- FIELDING, LEONARD T.  
Minneapolis General Hospital  
Minneapolis, Minnesota
- FINKELSTEIN, JOEL  
Cook County Hospital  
Chicago, Illinois
- FLAIG, ROBERT D.  
Minneapolis General Hospital  
Minneapolis, Minnesota
- FLANAGAN, KATHLEEN R.  
University of Michigan Hospital  
Ann Arbor, Michigan
- FREMLAND, ALAN D.  
Chas. T. Miller Hospital  
St. Paul, Minnesota
- FREMLAND, HARRIET J.  
Chas. T. Miller Hospital  
St. Paul, Minnesota
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Portland, Oregon
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- HEGRENES, ROBERT L.  
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- HEGSTAD, THOMAS C.  
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Minneapolis, Minnesota
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Veterans Administration Hosp.  
Los Angeles, California
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- HOVER, LEON W.  
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New York City, New York
- HYLAND, LOWELL J.  
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- JACKMAN, ROGER J.  
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Torrance, California
- JOHANSON, WALDEMAR G.  
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Minneapolis, Minnesota
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Oakland, California
- LAKOSKY, RANDALL A.  
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St. Paul, Minnesota
- LAPLANTE, E. SCHRAE  
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- LANGNER, HERMAN P.  
Cook County Hospital  
Chicago, Illinois
- LARSON, PAUL H.  
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- LEAF, DONN S.  
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- LOGEMANN, RONALD L.  
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- MADDEN, PETER N.  
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Oakland, California

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- RANDALL, PHILIP S.  
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Chicago, Illinois
- REEM, RICHARD C.  
Cook County Hospital  
Chicago, Illinois
- RIERSON, PHILLIP A.  
Santa Clara County Hospital  
San Jose, California
- RIVKIN, LAURENCE S.  
Minneapolis General Hospital  
Minneapolis, Minnesota
- ROBBINS, THOMAS O.  
St. Mary's Hospital  
Duluth, Minnesota
- ROGENTINE, G. NICHOLAS  
Massachusetts General Hospital  
Boston, Massachusetts
- ROTH, ALBERT H.  
Bethesda Hospital  
St. Paul, Minnesota
- SCHUT, LAWRENCE J.  
St. Luke's Hospital  
Duluth, Minnesota
- SEBALD, JOHN R.  
Santa Clara County Hospital  
San Jose, California
- SEGAL, MARVIN S.  
Veterans Administration Hosp.  
Los Angeles, California
- SIEGEL, LEIGHTON G.  
Sacramento County Hospital  
Sacramento, California
- SMITH, DAVID G.  
Santa Clara County Hospital  
San Jose, California
- STENZEL, DONALD A.  
St. Mary's Hospital  
Minneapolis, Minnesota
- SUTHERLAND, JOHN E., JR.  
Bethesda Hospital  
St. Paul, Minnesota
- THORSTAD, WILLIS M.  
Breckenridge Hospital  
Austin, Texas
- THURSTON, GORDON L.  
St. Luke's Hospital  
San Francisco, California
- ULLRICH, PETER H.  
St. Luke's Hospital  
Duluth, Minnesota
- VAN DE RIET, LOWELL  
Mt. View Hospital, Pierce Co.  
Tacoma, Washington
- VANDERSTEEN, PAUL R.  
Minneapolis General Hospital  
Minneapolis, Minnesota
- WASSON, ROBERT D.  
Cook County Hospital  
Chicago, Illinois
- WENGLER, ROBERT A.  
Ancker Hospital  
St. Paul, Minnesota
- WILLSON, RICHARD A.  
Mary Fletcher Hospital  
Burlington, Vermont
- WOLF, JOHN K.  
Parkland Memorial Hospital  
Dallas, Texas
- WOOD, ROBERT C.  
Univ. of Washington Hospitals  
Seattle, Washington
- ZUMBRUNNEN, JAMES L.  
Cook County Hospital  
Chicago, Illinois

## DR. SPINK IS PRESIDENT-ELECT OF AMERICAN COLLEGE OF PHYSICIANS

Dr. Wesley W. Spink, Professor of Internal Medicine at the University of Minnesota Medical School, was installed as president-elect of the American College of Physicians on April 13, 1962. He will become president of the 11,000 member organization in 1963. Dr. Spink, noted for his work in brucellosis and control of infectious diseases, is the second Minnesotan in the



Wesley W. Spink

history of the College to be elected president. Dr. S. Marx White, pioneer Minneapolis internist and former head of the Department of Medicine at the University, was president in 1932, and is the oldest living ex-president of the College.

Dr. Spink has spent 25 years on the Medical School faculty. He is a graduate of Carleton College (1926) and the Harvard Medical School (1932). A native of Duluth, Minn., he joined the University of Minnesota faculty in August, 1937, as an assistant professor of medicine. He is a past president of the Minnesota Medical Foundation, (1955-58), the American Society for Clinical Investigation (1949), the Central Society for Clinical Research (1950), the Minnesota Pathological Society (1944), and is presently a Consultant in Internal Medicine to the U.S. Air Force. He is chairman of the Expert Committee on Brucellosis of the World Health Organization.

Dr. Spink, 57, received an honorary Doctor of Science degree from Carleton College in 1950, and received the 1953 distinguished service award of *Modern Medicine* for contributions to study of brucellosis.

## DIVISION OF CANCER BIOLOGY IS DISCONTINUED

The Cancer Biology division of the University of Minnesota Medical School has been discontinued, Dr. Robert B. Howard, Dean, announced. The University's Board of Regents approved the change effective April 1, 1962. The division was directed by Dr. John J. Bittner, one of the nation's outstanding cancer scientists, who died on December 14, 1961.

"The division was very much identified with Dr. Bittner," Dr. Howard said, "and with his death there is no one who is doing exactly the same type of work. Therefore, continuing the division of cancer biology did not seem appropriate."

The two other faculty members of the division—Dr. Franz Halberg and Dr. Herbert Hirsch—have been transferred to the Department of Pathology and appointed professor and associate professor of experimental pathology, respectively.

### AMERICAN ASSOCIATION OF ANATOMISTS HOLDS ANNUAL MEETING IN MINNEAPOLIS

The Department of Anatomy and the University of Minnesota were hosts to the 75th annual meeting of the American Association of Anatomists held March 20-23 at the Leamington Hotel in Minneapolis. Approximately 1,200 medical scientists attended the meeting, held in the Twin Cities for the first time since 1917.

Dr. Charles F. Morgan, Professor of Anatomy at the Medical School, served as general chairman of the convention, and was assisted by members of the Department of Anatomy staff. A number of Minnesota faculty members were among authors of the 334 scientific papers which were presented. Dr. Arnold Lazarow, Professor and Head of the Department of Anatomy, was guest editor of the March 1962 issue of *Journal-Lancet*, devoted entirely to the topic of anatomy.

## Memorial Gifts

Memorial gifts to the Minnesota Medical Foundation have been received recently in memory of:

**Ann Dorothy Miller**  
Minneapolis, Minn.

**Mr. and Mrs. Carl Norman**  
Minneapolis, Minn.

**Mr. James Zwickl**  
Minneapolis, Minn.

Memorial contributions are a practical means of honoring the memory of a friend or loved one, while helping the Minnesota Medical Foundation in the advancement of medical education and research. Appropriate acknowledgements are promptly sent to both donor and family of the deceased.

## Medical Foundation News

### FOUNDATION GIVES FIRST ENDOWED RESEARCH AWARDS

The Minnesota Medical Foundation has announced distribution of the first medical research awards made available through a major legacy which it received in 1961. Three members of the University of Minnesota Medical School faculty will share a total of \$4,000 granted for the initiation of new projects in the fields of heart disease and cancer.

Dr. B. F. Woolfrey, instructor in pathology, was awarded \$1,500 to begin a study aimed at development of an autoradiographic method of localizing enzyme activities of tissue sections.

Dr. Demetre M. Nicoloff, medical fellow specialist in surgery, received \$1,500 to investigate the effects of certain drugs on the problem of atherosclerosis.

Charles H. Blomquist, teaching assistant in the Department of Physiological Chemistry, was granted \$1,000 to study hormone activity in heart muscle cell cultures.

The new grants are made possible by a permanent endowment fund created from a \$200,000 bequest for heart disease and cancer research made to the Minnesota Medical Foundation. The donor was the late Arvid Olson, a North Dakota merchant and farmer who died in 1957. The Foundation uses the fund to provide local support for young medical researchers in the initiation of meritorious projects which cannot be financed through primary sources, according to Eivind Hoff, Jr., executive secretary.

The Foundation is a voluntary organization of 2,000 doctors and laymen who encourage and provide certain types of private support for the University of Minnesota Medical School. Dr. Arnold Lazarow, professor and head of the Department of Anatomy, is president.

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## Alumni Notes

◆ 1941

**Winfred H. Clarke**, orthopedic surgeon in Portland, Ore., was named chief of the medical staff at Providence Hospital. He is also a clinical instructor at the University of Oregon Medical School.

◆ 1943

**Clark W. Truesdale** was elected mayor of Glencoe, Minn., on March 13, 1962. He has practiced medicine in that city for nearly two decades.

◆ 1947

**Maurice N. Johnson** was named assistant medical director of the Monsanto Chemical Co., St. Louis, Mo.

◆ 1949

**William Inglis**, Redwood Falls, Minn. physician, was elected president of the University of Minnesota Alumni Club in that city.

◆ 1951

**Robert T. Kelly**, Grand Rapids, Minn., is president of the Range Medical Society for 1962. Other officers are **H. Wayne Johnston**, (Med. '52), Virginia, vice-president; **Richard E. Barnes** (Med. '52), Aurora, president-elect; and **George B. Ewens** (Med. '53), Virginia, secretary-treasurer.

◆ 1956

**David I. Gottlieb** has received his discharge from the U.S. Navy. He was formerly stationed at the U.S. Naval Hospital, San Diego, Calif., as a medical officer.

**John C. Richards** was awarded the degree of Master of Science in general surgery from the University of Minnesota. He took his training at the Mayo Foundation, Graduate School, Rochester, Minn.

◆ 1959

**Carl Gustav Evers** is now on active duty with the U.S. Army with the 134th Mobile Surgical Hospital at Ft. Polk, La. Dr. and Mrs. Evers are parents of a daughter, Karen Alicia, born January 2, 1962. Mrs. Evers is the former Janella Magee, Tylertown, Miss. They were married July 10, 1960. Upon completion of military service, Dr. Evers plans to return to the University of Mississippi Medical Center to continue his residency training in pathology. The family presently resides at 4325 Azalea Drive, Jackson, Miss.



J. C. RICHARDS

◆ 1960

**Robert L. Johnson** is now a Lieutenant in the U.S. Navy Medical Corps, and is on duty aboard the transport vessel USS GENERAL W. A. MANN.



P. J. SCANLAN

**Charles Keenan** has become affiliated with the Ross-Loos Medical Group and is now in practice at 2515 Wilshire Blvd., Santa Monica, Calif.

◆ 1961

**Patrick J. Scanlan** will begin a residency in Obstetrics-Gynecology on July 1, 1962, at the University of Minnesota Hospitals. He is completing his internship at St. Mary's Hospital, Duluth, Minn.

SENIOR CLASS-ALUMNI LUNCHEON

The Minnesota Medical Alumni Association will again sponsor the Senior Class-Alumni Luncheon on Thursday, May 3, 1962, at the Coffman Union, University of Minnesota. Dr. Charles J. Beck, (Med. '40) North St. Paul, Minn., is president of the group, which annually honors the graduating class in medicine.



HAROLD G. SCHEIE

Luncheon speaker will be Dr. Harold G. Scheie (Med. '36), Professor of Ophthalmology at the University of Pennsylvania College of Medicine. His topic will be "Changing Trends in Medicine." Medical alumni and faculty are invited to sponsor a senior medical student and to attend the luncheon.

ALUMNI DEATHS

◆ 1903

**Dr. Olin W. Rowe**, pioneer pediatrician in Duluth, Minn., died February 20, 1962 in that city. He was 80 years old and had retired in 1959. Dr. Rowe was one of the founders of the Duluth Clinic, and had served as chief of staff of all three Duluth hospitals. In 1953 he was honored by the Minnesota State Medical Association on completion of fifty years of medical practice.

◆ 1919

**Dr. R. J. Carroll Brown** died March 5, 1962 in St. Peter, Minn., at the age of 69 years. A native of Nebraska, he had been a resident of Minneapolis for fifty years, where he had been in general practice. Survivors include a brother, **Dr. W. D. Brown (Med. '24)** of Minneapolis.

◆ 1930

**Dr. Victor E. Johnson**, Yakima, Wash., died December 19, 1961 of coronary occlusion. He was 58 years old. Dr. Johnson was a member of the American Academy of General Practice.

◆ 1940

**Dr. Theodore J. Keskey** of Ironwood, Mich., died January 14, 1962 at the age of 57. Death was caused by acute coronary thrombosis. He was a member of the American Medical Association, the medical staff of Grand View Hospital, Ironwood, and a veteran of World War II.

◆ 1945

**Dr. John Walker MacDonald**, a Minneapolis radiologist, died March 27, 1962 at the age of 40 years. He was a member of the American Medical Association and national and international radiological organizations. Survivors include his wife, Emmy-Lou, two sons, and one daughter. The family home is at 6633 Parkwood Road, Edina, Minn.

THE MEDICAL BULLETIN

NOTIFICATION OF CHANGE OF ADDRESS

PLEASE TYPE OR PRINT

NAME \_\_\_\_\_

\_\_\_\_\_

PRESENT ADDRESS \_\_\_\_\_

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Detach this sheet and mail to:

Minnesota Medical Foundation  
1342 Mayo Mem. Bldg.  
University of Minnesota  
Minneapolis 14, Minnesota

# Coming Events

University of Minnesota Medical School

## List of Continuation Courses for Physicians

University of Minnesota  
Center for Continuation Study

1962

- All Year . . . . . Cancer Detection for General Physicians  
April 12-14 . . . . . Otolaryngology for General Physicians  
April 16-18 . . . . . Internal Medicine for Internists  
April 26-28 . . . . . Surgery for Surgeons  
April 30-May 2 . . . . . Gynecology for General Physicians  
May 7-9 . . . . . Ophthalmology for Specialists  
May 14-18 . . . . . Proctology for General Physicians  
May 31-June 2 . . . . . Psychiatry for General Physicians

The University of Minnesota reserves the right to change this schedule without notification.

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Courses are held at the Center for Continuation Study or the Mayo Memorial Auditorium on the campus of the University of Minnesota. Usual tuition fees are \$30 for a two-day course, \$50 for a three-day course, and \$75 for a one-week course.

Specific announcements are sent out about two months prior to each course to all members of the Minnesota State Medical Association and to any physicians who request information for a specific course. For further information write to:

DIRECTOR  
DEPT. OF CONTINUATION MEDICAL EDUCATION  
THE MEDICAL CENTER  
UNIVERSITY OF MINNESOTA  
MINNEAPOLIS 14, MINNESOTA

# Memorial Gifts

Memorial gifts are popular means of paying thoughtful tribute to the memory of a relative, friend, or colleague.

Your Minnesota Medical Foundation welcomes memorial gifts, and makes immediate acknowledgment to the family of the deceased, and to the donor.

Contributions are used to help finance the programs of medical education and research conducted by the Minnesota Medical Foundation in behalf of the University of Minnesota Medical School.

Gifts may be sent to:

**Minnesota Medical Foundation  
1342 Mayo Memorial Building  
University of Minnesota  
Minneapolis 14, Minnesota**



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