THE RHEOLOGY OF BLOOD-EFFECT OF HEMATOCRIT AND TEMPERATURE ON YIELD VALUE

by

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Professor Philip Franklin
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Dear Sir:

The thesis entitled "The Rheology of Blood -- Effect of Hematocrit and Temperature on Yield Value" is herewith submitted in partial fulfillment of the requirements for the degree of Bachelor of Science.

Respectfully submitted,

Hyunkook Shin

ACKNOWLEDGEMENT

The author wishes to express his gratitude to Professor E. W. Merrill, under whose direction this work has been performed, for his overall guidance, advice and suggestions; to Mr. G. Cokelet for his helpful comments in interpreting experimental data; and to Messrs. P. Gilinson, C. R. Dauwalter, and J. Scoppettuolo for the use of their G.D.M. Viscometer.

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TABLES AND FIGURES

I. SUMMARY

The rheological properties of blood were studied in this investigation employing a Couette-type G.D.M. Viscometer. The range of shear rate of this instrument was from 0.02 sec^{-1} up to 100 sec^{-1}. Particular attention was given to the effect of hematocrit and temperature on the yield value of blood.

It was found that whole blood possesses yield value above a certain critical hematocrit. The critical hematocrit varied slightly for different blood samples depending on the plasma compositions, but it was in the range between 1.0% and 7%.

The yield value was found to increase rapidly with increasing hematocrit. Below an hematocrit of about 50%, the yield value and hematocrit could be best correlated by the equation

$$\tau_y^{1/3} = A\ (\ H - H_c\ )$$

and above 50%, by the equation

$$\tau_y = D\ e^{BH}\ .$$

The yield value appeared to be independent of temperature in blood samples having an hematocrit below 30%. Above 30%, the yield value seemed to increase slightly with decreasing temperature.

Red cells in the blood of a healthy person tend to form rod-like aggregates called rouleaux. If the blood

is left at rest, rouleaux tend to join one another to form a continuous network. This network is believed to give blood a rigid structure which is responsible for its plasticity and its yield value.

Because of the similarity of the rheological structure of blood to that of the Casson model, the relationship between the shear stress and the shear rate of blood could be best expressed by the Casson equation,

$$\sqrt{\tau} = a\sqrt{\dot{\gamma}} + b \ . \qquad (2)$$

Consequently, all yield values in this investigation were obtained from the Casson Plot.

The temperature effect on the viscosity of whole blood was also studied. The apparent viscosity was found to increase rapidly as temperature fell. However, the relative viscosity of blood, which is defined as the ratio of the viscosity of blood at any temperature to the viscosity of water at the same temperature, did not change very much with temperature above 20 ^{o}C. Below 20 ^{o}C the relative viscosity began to increase appreciably as temperature decreased.

Fibrinogen is believed to be responsible for the yield value of blood. A study on the rheological properties of the red cell suspensions in the fibrinogen solution is recommended for the future study.

II. INTRODUCTION

(A) Background and Objectives

Blood is probably the most important fluid of biological interest. It has the functions, first of conveying oxygen from the lungs to the tissues and of returning carbon dioxide from the tissues to the lungs, secondly of supplying tissues throughout the body with the oxidisable food materials derived from the digestive tract, and of returning the products of metabolism from the tissues to the excretory organs.

The purposes of this investigation were the following: 1) to determine whether or not blood possesses a yield value, that is, a minimum shear stress that must be applied before flow can begin; 2) to determine the effect of hematocrit (the volume percent of red cells) and temperature on the yield value of blood if it exists.

During the last several decades the rheological properties of blood have been investigated by many workers. It has been generally recognized that the viscosity of whole blood increases as the shear rate decreases or as the hematocrit increases (1, 2, 3, 4, 5).

However, there has been little comprehensive work done on the yield value of blood. Furthermore, the few existing

articles dealing with the subject do not agree.

It is of profound importance to the physiologists whether or not blood possesses a yield value, for at least two reasons; Firstly the yield value might contribute to the critical closing pressure in the vessels of microcirculation; secondly, quantitative information on the yield value will aid the understanding of the rheological structure of the whole blood. The study of the rheological properties of blood is of interest to chemical engineers because of its similiarity to pigment-oil suspensions, kaolin suspensions, and other industrial fluids, and because of the interest inherent in applying chemical engineering concepts to a major medical problem.

Copley and his co-workers appear to be the first who claimed that whole blood possesses a yield value (6). His experiment was performed with a rolling ball viscometer (a modified falling ball viscometer). He calculated, instead of the absolute yield value in the units of dynes/cm^2, the gravity force in dynes required for the ball to start to roll down through the blood contained in a tube at same critical angle of the tube inclination. There is an indication in one of his recent publications that he still believes in the presence of a yield value in the whole blood (7): His plot of the square root of the shear stress

as the X-axis versus the square root of the shear rate as the Y-axis (Casson Plot) cuts the X-axis on the positive side indicating the presence of a yield value. Scott Blair also made a Casson Plot extrapolating to a yield value of about 16 dynes/cm^2 (8).

Haynes and Burton, on the other hand, believe that blood does not have any yield value (9, 10). Their claim is based on a rather extensive investigation of red cell-saline suspensions using capillary viscometers.

Most of the workers who studied the rheological properties of blood employed capillary viscometer (4, 5, 8, 9, 10). The disadvantage of this viscometer is that it is not suited for measurements at low shear rates, the region which is critically important in determining whether or not a yield value exists. The fact that Scott Blair did not explicitly claim the presence of a yield value in the whole blood seems to indicate that he was aware of the importance of the low shear rate region which he could not reach with his capillary viscometer.

Since Burton and Haynes based their conclusion on data obtained at relatively high shear rates (i.e., above 10 1/sec.), the validity of their conclusion is very questionable.

All rheologists now agree that the apparent viscosity of

blood decreases with increasing temperature. However, there is some confusion about the effect of temperature on the "relative viscosity of blodd" which is defined as the ratio of the viscosity of blood at any temperature to that of the viscosity of water at the same temperature. Some believe that the relative viscosity of blood decreases with increasing temperature (9, 11), whereas other believe that it is "practically" independent of temperature (12, 13). Furthermore there is a complete lack of systematic investigation on the temperature effect.

In this investigation, a Couette-type G.D.M. Viscometer (See Appendix A & B) was employed to determine whether or not blood possesses a yield value. The effects of temperature and hematocrit on the viscosity and on the yield value of blood also were considered. The G.D.M. viscometer utilizes the torque-to-balance loop, an electronic torque measuring device, which is capable of measuring a torque as small as one-thousandth of a dynes-cm. The range of shear rate of the instrument is from 0.02 1/sec. up to 100 1/sec.. A temperature controlling device, specially designed for this viscometer by Professor E.W. Merrill of the Chemical Engineering Department, M.I.T., can keep the temperature of the sample fluid constant at any desired temperature between about 15 ^{o}C and 100 ^{o}C.

(B) The Constitution of Blood

Blood is essentially a concentrated suspension of particles visible in the optical microscope (red cells, white cells and platelets). The suspending fluid consists of an aqueous salt solution of three major types of protein: albumin, globulin, and fibrinogen. All of these proteins are anisometric rigid macromolecules (1), visible in the electron microscope.

It is the suspended particles (the corpuscles) which are mainly responsible for the peculiar rheological properties of whole blood. Of these corpuscles, the red cells dominate in volume, occupying about 45 percent of the total volume of the normal blood. The shape of the red cells is that of a biconcave disc. Table 1 and Figure 1 summarize the constitution of blood, the shape of some of the important constituents of blood and their physical properties.

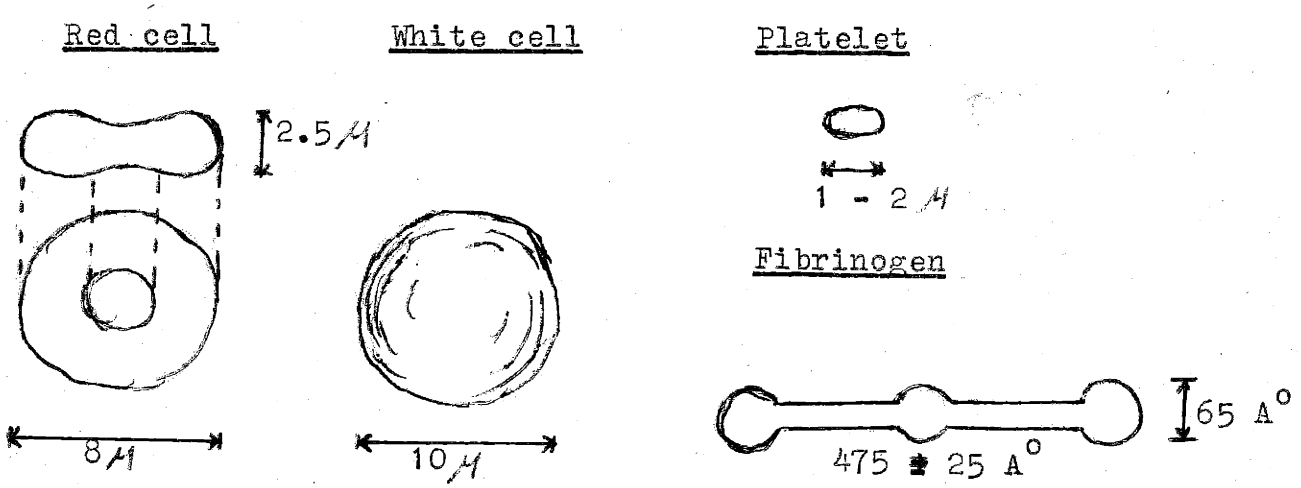


Fig. 1 Shape of corpuscles and fibrinogen (1)

TABLE 1. The Constitution of Blood (I)

A) Suspended Particles

Corpuscles	No. corpuscles/cc blood
Red cell	5 billion/cc
White cell	10 million
Platelet	500 million

B) Suspending fluid (plasma)

		gm/100cc.plasma	M.W.	Axis lengths as ellipsoids (°A)	
Protein	Albumin	3.5	67,000	150	50
	Globulin (α, β, γ)	2.5	150,000	245	44
	Fibrinogen	0.5	340,000	475	15 to 50
Salt	NaCl	0.86			
	KCl	0.03			
	$CaCl_2$	0.033			

(C) Newtonian and Non-Newtonian Viscosity

Viscosity is defined as the ratio of shear stress to the shear rate, thus

$$\tau = \eta \frac{du}{dr} = \eta \dot{\gamma} \qquad (1)$$

where τ = shear stress (dynes/cm^2)

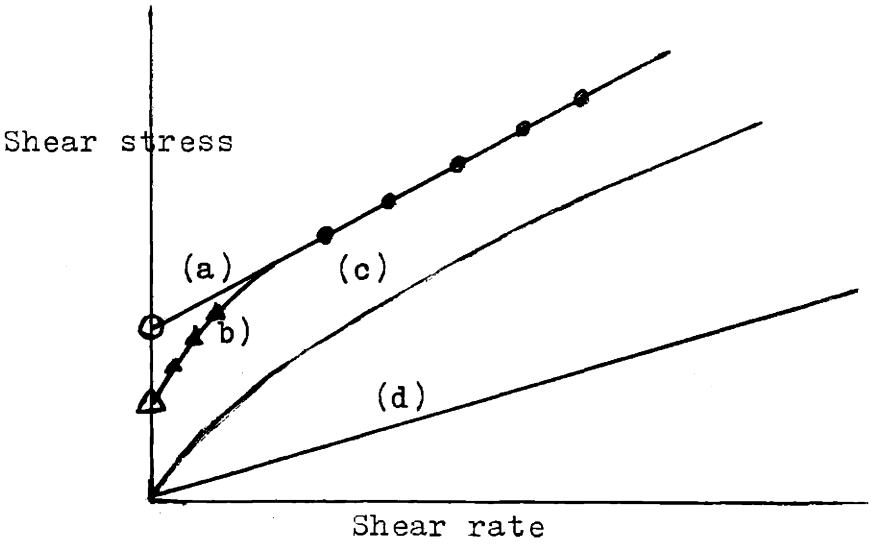
η = viscosity (poises)

and $\dot{\gamma}$ = du/dr = shear rate or velocity gradient (1/sec.)

Newtonian refers to a fluid which exhibits a constant viscosity independent of the shear rate. Water, benzene, and ethyl alcohol are therfore Newtonian fluids.

Non-Newtonianism, on the other hand, implies that viscosity changes as the shear rate changes. It occurs in most colloidal solutions and suspensions of particles.

To the non-Newtonian category belong the so-called pseudoplastic liquid, the simple Bingham liquid and the false yield Bingham liquid (14). Figure 2 illustrates the relationship between various types of fluids mentioned above.



(a) Simple Bingham liquid (b) False yield Bingham Liq.
(c) Pseudoplastic liquid (d) Newtonian liquid

Fig. 2 - Newtonian and Non-Newtonian Liquids

Blood, like pigment-oil suspensions, or kaolin suspensions, belongs to the category of false yield Bingham liquid.

(D) Plasticity, Elasticity, and Yield Value

Houwink is perhaps the one who studied the subject of yield value most extensively (15, 16). According to him, it is defined "as the smallest load under which a given substance will obtain a permanent deformation or will begin to flow". This means that if the stress applied is less than the yield value, the substance will undergo an "elastic deformation" which disappears entirely upon the release of the stress. If, however, the stress applied exceeds the yield value no complete recovery can be observed after release of the stress. In this case a "plastic deformation" is said to have occured.

Yield value clearly corresponds to the intercept on the stress-axis in Figure 2. However extrapolation of data to obtain a yield value can be inaccurate even in order of magnitude. For example in Figure 2, if the only data available are that shown as solid circles, extrapolation would lead to a yield value shown in the open circle. But if data are obtained at lower shear rates (solid triangles), it is often found that there is a pronounced curvature

toward the origin and the real yield value (open triangle) lies far below the false one (open circle). Bolger (17), among others has studied these interrelationships. Generally, capillary viscometers operate at such a level of shear rate that they give only the linear portion of a false yield Bingham fluid. A coaxial cylinder viscometer is usually necessary to determine the low shear rate, curved part of the relation, indicated by triangles in Figure 2.

A generally important type of false yield Bingham fluid is found with suspensions in which the particles reversibly aggregate into rod-like structures. Casson (18) derived an equation which relates shear stress to shear rate for the suspension of chain-like floccules present in varnishes and printing inks. In deriving his flow equation Casson assumed that attractive forces are present between particles and between long rigid floccules whose length increases by collisions and decreases as shear stress increases, that the suspending fluid is a Newtonian liquid and that Brownian effects are negligible. His final equation may be written in its simplest form as

$$\sqrt{\tau} = a\sqrt{\dot{\gamma}} + b \qquad (2)$$

where a and b are constants to be dtermined experimentally.

Since the plot of $\sqrt{\tau}$ versus $\sqrt{\dot{\gamma}}$ gives a straight line for

false yield Bingham liquid, the yield value can be easily determined by extrapolation of experimental data. The square of the intercept on the $\sqrt{\tau}$ axis, that is b^2, is nothing but the yield value.

(E) The Effect of Temperature on Viscosity and on Yield Value

The temperature dependence of viscosity can usually be expressed by the simple equation

$$\eta = A\, e^{E/kT}$$

where η = viscosity

E = potential energy

T = absolute temperature

and k = Boltzmann constant

This equation was first obtained by Andrade (19)$_b$ in 1930. He deduced this equation by assuming that, if the potential energy of the adjacent molecules is E, then the probaility that two molecules will join each other is proportional to $e^{E/kT}$.

Although simple, this equation is found to be remarkably correct for many fluids. Therefore when $\log \eta$ is plotted against $1/T$, a straight line or a line close to a straight line is usually obtained for many fluids.

There is, however, no general expression for the temperature effect on the yield value. For amorphorous substances (Selenium and colophony), it was found that the relationship between the yield value and the temperature could be approximated by the equation

$$\tau_y = A\, e^{B/T} \qquad (4)$$

above a certain temperature (i.e. 20 °C), below which, however, the yield value was found to be independent of temperature (15). A and B in the above equation are constants.

For a clay paste of 50%, the investigation by Wolarowitch and Tolstoi shows that the yield value is independent of temperature between 10 °C and 57 °C (15). Houwink believes that the yield value for clay paste actually decreases as temperature increases, but the change was too small to be detected in the experiments. He estimated the magnitude of the temperature effect on the yield value by considering the change in the potential energy in the electrical double layer.

III. PROCEDURE

A portion of blood was transferred into a tube and was centrifuged for twenty minutes at 3,000 RPM. The centrifuge employed was equipped with a built-in refrigerating system, which maintained the temperature of the blood sample at about 3 ^{o}C throughout the period of centrifuging.

A clear yellowish plasma at the top and red cells at the bottom were seperated with the use of a syringe. Blood samples at different hematocrits were prepared by adding either plasma or red cells to the original sample.

About 8.5 cc of the sample thus prepared was then placed in the viscometer cup, and the bob of the viscometer head was introduced carefully into the sample. The system was brought to some desired temperature by adjusting the temperature control screw in the Haake thermostat, which circulates liquid of a constant temperature inside the silver bob of the viscometer head. The equilibrium of temperature was attained fairly rapidly owing to the large thermal conductivity of silver.

In order to correct for the possible zero shift in the torque scale, the bob was made to rotate first in the clockwise direction and then in the counterclockwise direction. Consequently two torque readings were obtained at each RPM. The average of the two readings gave the actual

torque at the given RPM. Equations used for the calculation of shear stress and shear rate from torque and the rotational speed respectively will be given in VIII APPENDIX (A).

Below 2 RPM, blood sample in the cup was always stirred up before taking a reading by moving the viscometer head up and down several times. The purpose of doing this was to minimize the wall effects by eliminating the marginal plasma layer (See V DISCUSSION A).

Two Inscomotors were employed to vary rotational speed of the bob from 0.02 RPM up to 100 RPM. Determination of hematocrits was done by centrifuging 1 cc of blood sample in the Winthrop tube for 30 minutes at 5,000 RPM.

IV. RESULTS

(A) Effect of Hematocrit on the Yield Value of Whole Blood

Three series of runs were made in this investigation to determine the effect of hematocrit on the yield value.

Figures 3 and 4 illustrate how shear stress increases with increasing hematocrit at a given shear rate in the regions of low shear rate (0.1 to 2 1/sec.) and high shear rate (2 to 100 1/sec.) respectively. The intercepts on the y-axis in Figure 3 correspond to the yield values at various hematocrits. From these plots it is clear that the yield value increases with increasing hematocrit.

In order to obtain the yield value more accurately, Casson plots were made for all three series of runs (Figures 5, 6, and 7). Yield values at various hematocrits, calculated from the intercepts of Casson plots, were then tabulated in Table 2. The results indicate that the yield value increases much more rapidly than hematocrit, throughout the range of hematocrit investigated.

A plot of $\log(\tau_y)$ versus hematocrit (Figure 7) further indicates that the change in yield value induced by the change in hematocrit is greater at lower hematocrits.

In correlating the experimental results, it was found

that the yield values of whole blood fit the equation

$$\tau_y = A (H - H_c) \qquad (7)$$

up to an hematocrit of about 50% (Figure 9),. Here A is a constant in the units of $(\text{dynes})^{1/3}$ and H_c is the critical hematocrit at which the yield value first appears. From Figure 9, the constant A and the critical hematocrit H_c was obtained for the three series of runs made:

$$\text{Series I} : (\tau_y)^{1/3} = 0.0073 (H - 7.0) \qquad (8)$$

$$\text{Series II} : (\tau_y)^{1/3} = 0.0092 (H - 1.5) \qquad (9)$$

$$\text{Series III}: (\tau_y)^{1/3} = 0.0073 (H - 2.0) \qquad (10)$$

TABLE 2 Yield Value at Various Hematocrits

Series I.

Hematocrit	$\sqrt{\tau_y}$	$\sqrt[3]{\tau_y}$	τ_y
52.4	.184	.324	.0338
36.4	.1	.215	.01
33.2	.086	.195	.0074
30.0	.069	.168	.00476
22.8	.040	.117	.0016
19.0	.023	.081	.000529
12.1	.008	.040	.000064
0	-	-	-

Series II.

Hematocrit			
64.3	.364	.510	.1325
38.8	.20	.342	.040
31.6	.145	.276	.021
25.1	.116	.237	.01345
18.6	.065	.162	.00423
10.6	.024	.083	.000576
7.2	.013	.055	.000169

Series III.

Hematocrit	$\sqrt{\tau_y}$	$\sqrt[3]{\tau_y}$	τ_y
45.4	.179	.318	.0320
31.1	.094	.207	.00883
22.0	.052	.149	.002705
10.8	.018	.0688	.000324
6.81	.007	.0365	.000049

(B) Effect of Temperature on the Viscosity and Yield Value of Whole Blood

The viscosity of whole blood could be correlated to temperature by the Andrade equation fairly well down to 24 °C. Below 24 °C, however, the actual viscosity was found to be slightly higher than that predicted by the equation. In other words, when ln η was plotted against 1/T, a fairly good straight line was obtained down to 24 °C. Below 24 °C, the ln η - 1/T curve bends upward slightly. It was also noticed that the ln η - 1/T curves for different shear rates were approximately parallel to one another (Figure 10A).

In Figure 10B, the relative viscosity of whole blood (η blood/η water), presented in Table 3, was plotted against temperature. It was found that , above 20 °C, the relative viscosity did not change very much with temperature. Below 20 °C, however, the relative viscosity increased appreciably with decreasing temperature. Such an increase in relative

viscosity was more pronounced at low shear rates.

TABLE 3. The Relative Viscosity of Whole Blood at various Temperatures

Hematocrit=41.3

Temp (°C)	Shear Rates	Viscosity of Whole Blood (η_B cp) 2	5	20	100	Viscosity of Water (cp)
14.02	η_B	22.5	16.3	10.8	7.65	1.171
	η_B/η_{H_2O}	19.2	13.92	9.22	6.53	
20.25	η_B	16.6	12.3	8.75	6.3	0.999
	η_B/η_{H_2O}	16.6	12.3	8.75	6.3	
23.65	η_B	15.0	11.2	8.05	5.75	0.922
	η_B/η_{H_2O}	16.3	12.15	8.74	6.24	
27.05	η_B	13.9	10.4	7.25	5.20	0.854
	η_B/η_{H_2O}	16.3	12.19	8.50	6.09	
38.00	η_B	10.45	8.20	5.75	4.07	0.681
	η_B/η_{H_2O}	15.35	12.04	8.44	5.97	

The temperature effect on yield value was studied in the experiments of Series II. Each run in the series was made at three different temperatures: 19 °C, 25 °C, and 37 °C. The yield value appears to be independent of temperature for blood samples having a hematocrit below about 30%, above 30%, the yield value seems to increase with decreasing temperature by a very small amount (i.e., approximately 12% for a blood of hematocrit = 64.3 between 19 °C and 37 °C) (Figure 11).

(C) Effect of Shear Rate and Hematocrit on Viscosity

A plot of viscosity versus shear rate indicates that for a normal blood (H=45%) viscosity increases from about 10 c_p to about 80 c_p as shear rate decreases from 10 sec^{-1} to 0.1 sec^{-1} (Figure 12). It is to be noticed that most of the increase in viscosity occurs below 1 sec^{-1}. The viscosity of plasma, on the other hand, was independent of shear rate. Plasma was thus found to be a Newtonian fluid.

Bayliss claimed that a plot of relative viscosity (the ratio of the viscosity of blood to that of plasma) against $1/\left(1 - \left(\frac{H}{100}\right)^{\frac{1}{3}}\right)$ gave a straight line for blood (4). Data from the experiments of Series III were plotted on such a plot (Figure 13). At high shear rate, a straight line could be drawn through the data points. But as the shear rate falls below 10 sec^{-1}, the curve bends upward as hematocrit increases.

(D) Blood of a Sick Person

In Figure 14, Casson plots made for blood from a healthy person and from a sick person are shown. One interesting difference of the two is that blood from a sick person does not possess any yield value. Two curves in group 1 also illustrates the effect of oxygen content in the gas phase

in equilibrium with blood. Higher oxygen concentration in the gas phase was found to lower the viscosity of blood. Two curves in group 2 show the effect of heparin on the viscosity.

This experiment seems to indicate that heparin lowers the viscosity of blood. This finding, however, is not conclusive. In other experiments performed for this investigation, the effect of heparin on viscosity was hardly detectable.

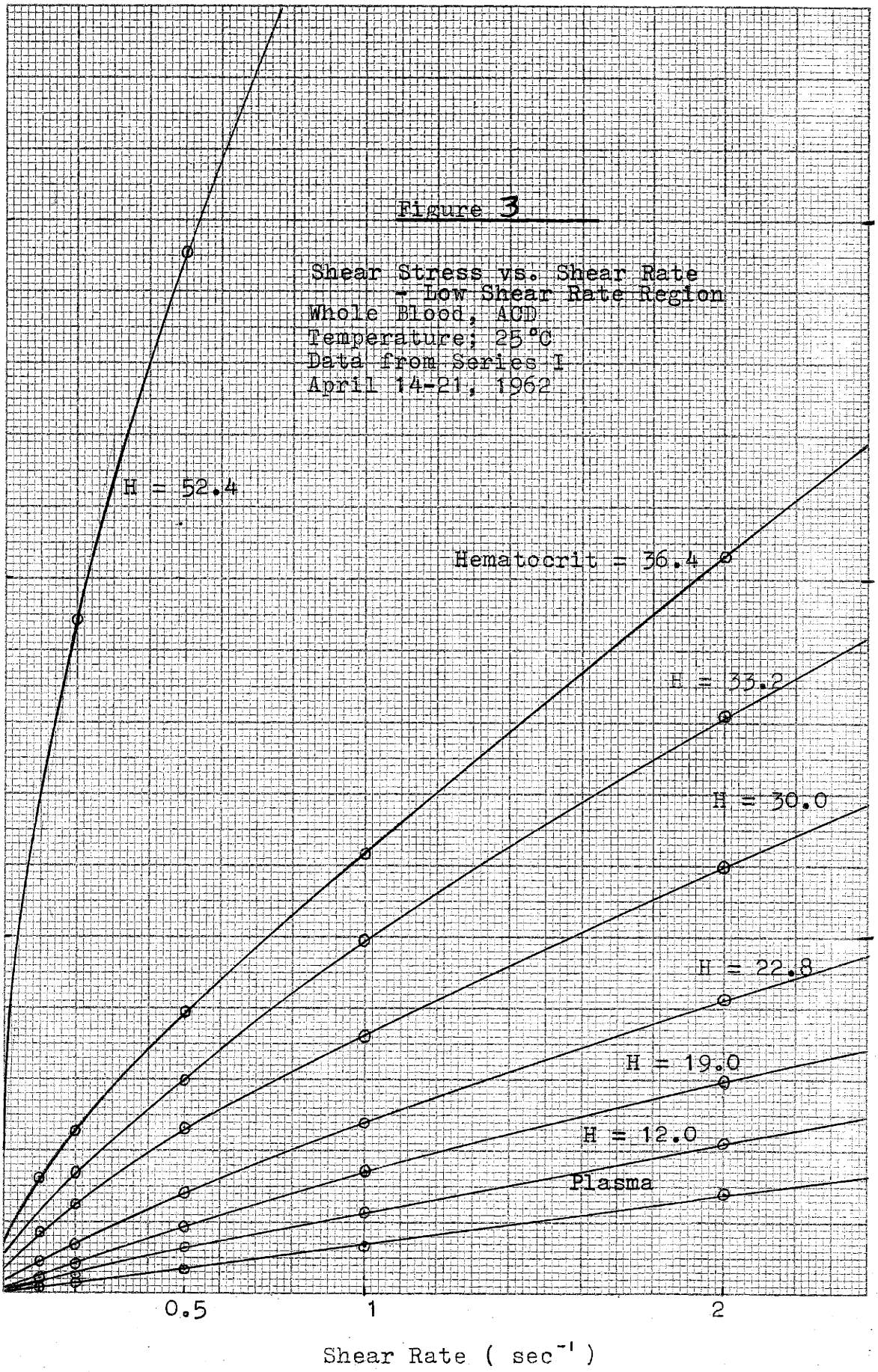


Figure 3
Shear Stress vs. Shear Rate
- Low Shear Rate Region
Whole Blood, ACD
Temperature; 25°C
Data from Series I
April 14-21, 1962
H = 52.4
Hematocrit = 36.4
H = 33.2
H = 30.0
H = 22.8
H = 19.0
H = 12.0
Plasma
0.3
0.2
0.1
0.5
1
2
Shear Stress (dynes / cm²)
Shear Rate (sec⁻¹)

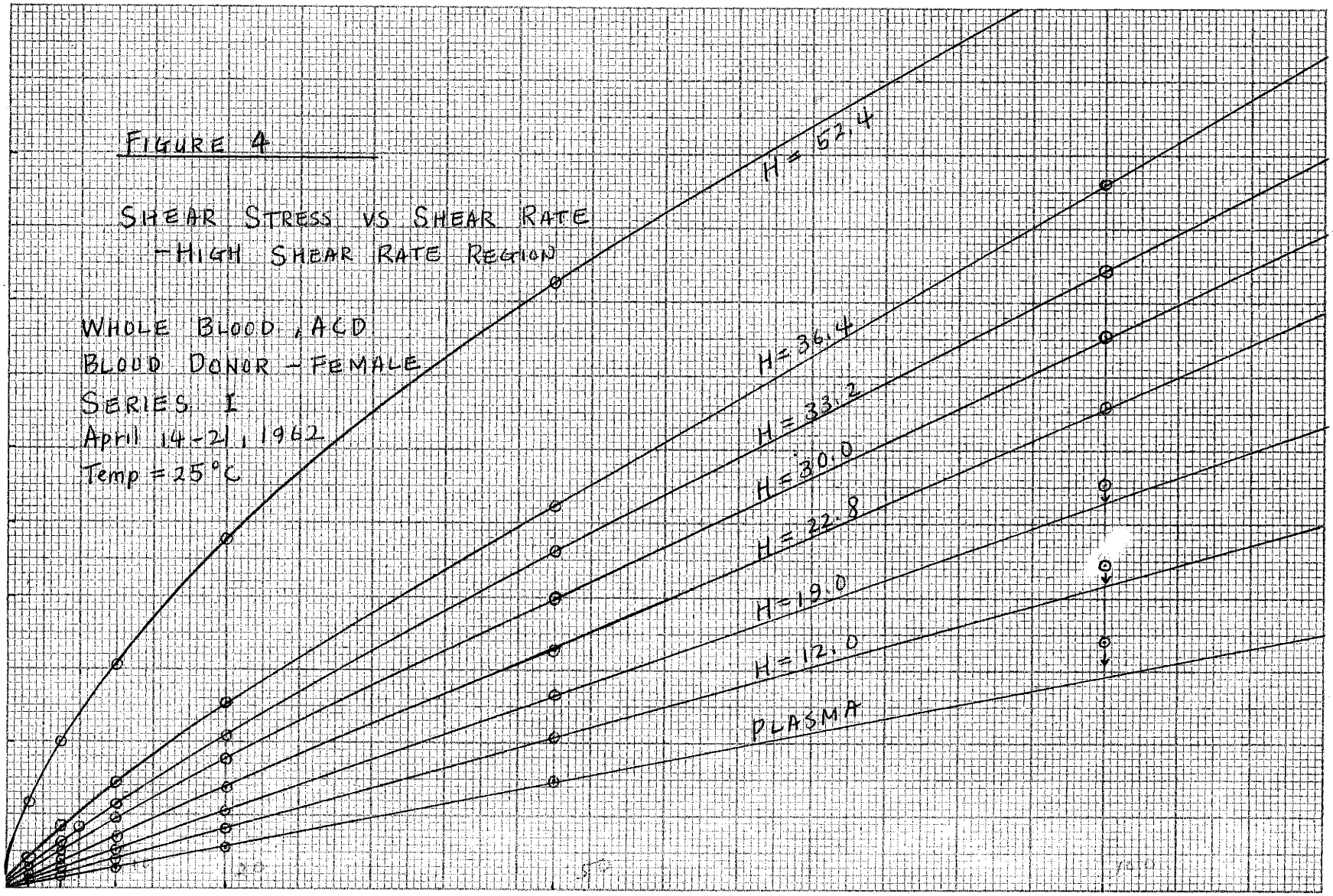


FIGURE 4
SHEAR STRESS VS SHEAR RATE
-HIGH SHEAR RATE REGION
WHOLE BLOOD, ACD
BLOOD DONOR - FEMALE
SERIES I
April 14-21, 1962
Temp = 25°C
H = 52.4
H = 36.4
H = 33.2
H = 30.0
H = 22.8
H = 19.0
H = 12.0
PLASMA
SHEAR STRESS (dynes/cm²)
SHEAR RATE (SEC⁻¹)
1
2
3
4
5
10
20
50
100

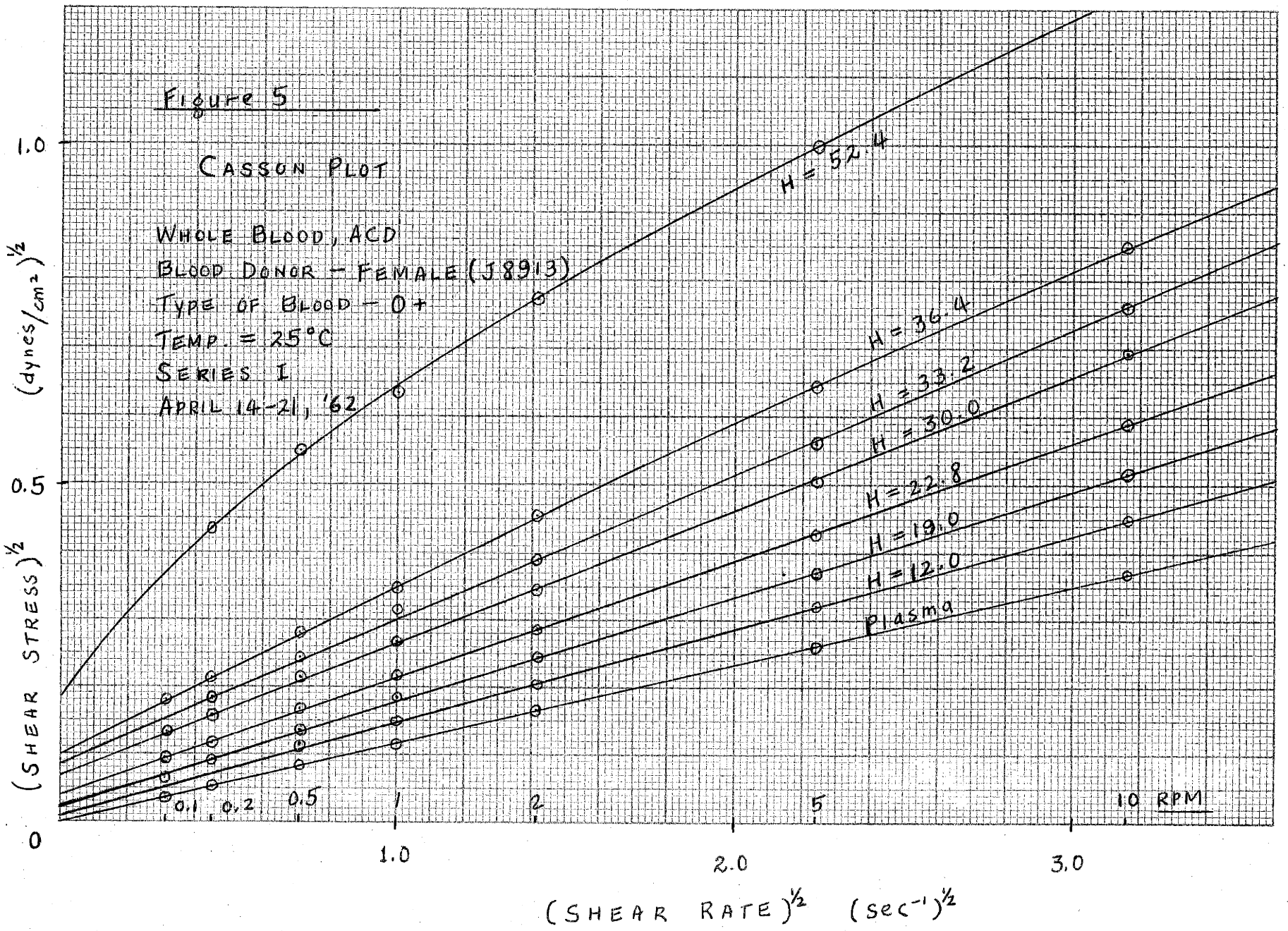


Figure 5
CASSON PLOT
WHOLE BLOOD, ACD
BLOOD DONOR - FEMALE (J8913)
TYPE OF BLOOD - O+
TEMP. = 25°C
SERIES I
APRIL 14-21, '62
H = 52.4
H = 36.4
H = 33.2
H = 30.0
H = 22.8
H = 19.0
H = 12.0
Plasma
0.1
0.2
0.5
1
2
5
10 RPM
1.0
0.5
0
1.0
2.0
3.0
(SHEAR STRESS)½ (dynes/cm²)½
(SHEAR RATE)½ (sec⁻¹)½

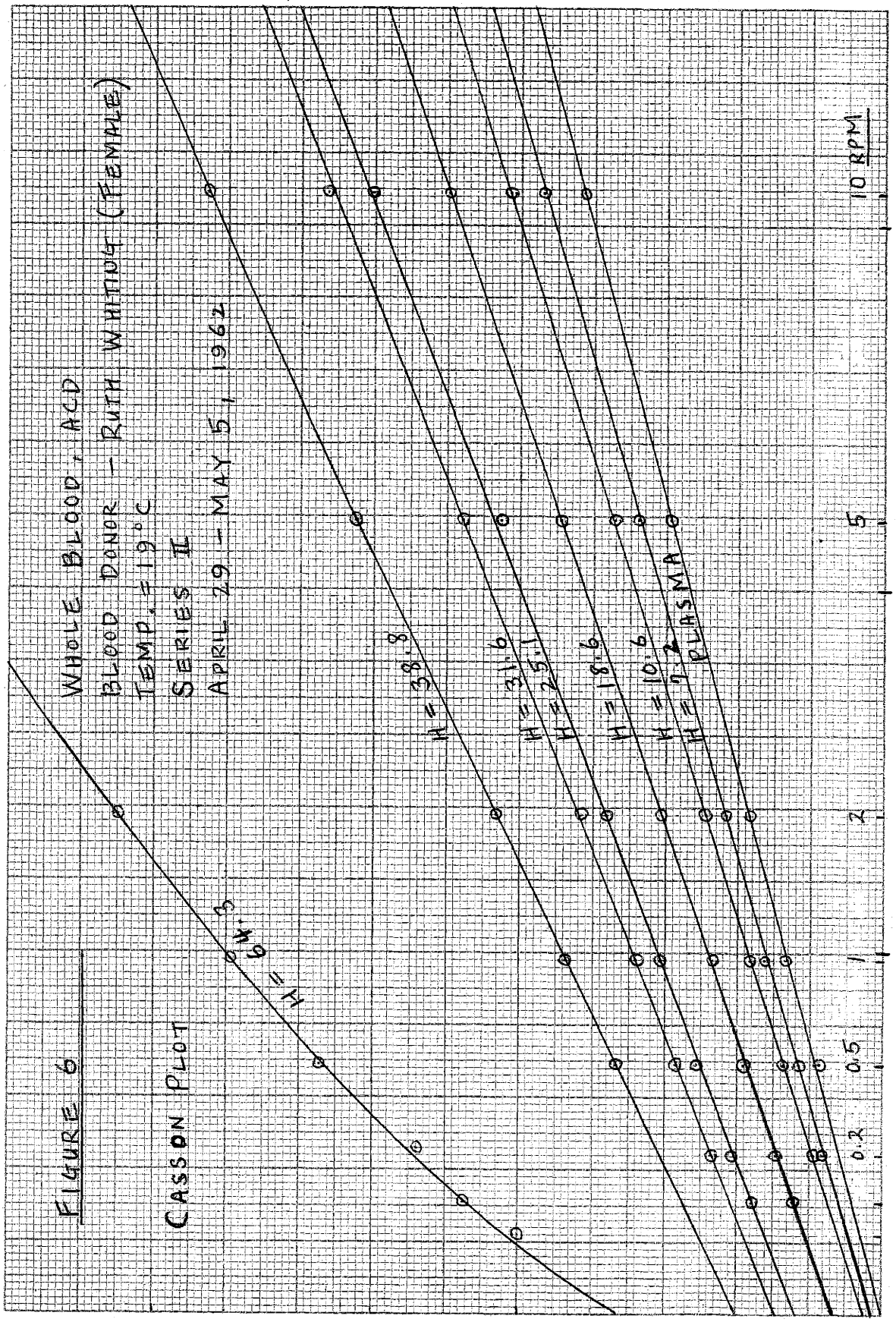


FIGURE 6
WHOLE BLOOD, ACD
BLOOD DONOR — RUTH WHITTIG (FEMALE)
TEMP. = 19°C
SERIES II
APRIL 29 - MAY 5, 1962
CASSON PLOT
H = 38.8
H = 31.6
H = 25.1
H = 18.6
H = 10.6
H = 5.2
PLASMA
10 RPM
1.0
0.5
2.0
3.0
0.2
0.5
1
2
(SHEAR STRESS, dynes/cm²)^½
(SHEAR RATE, SEC⁻¹)^½

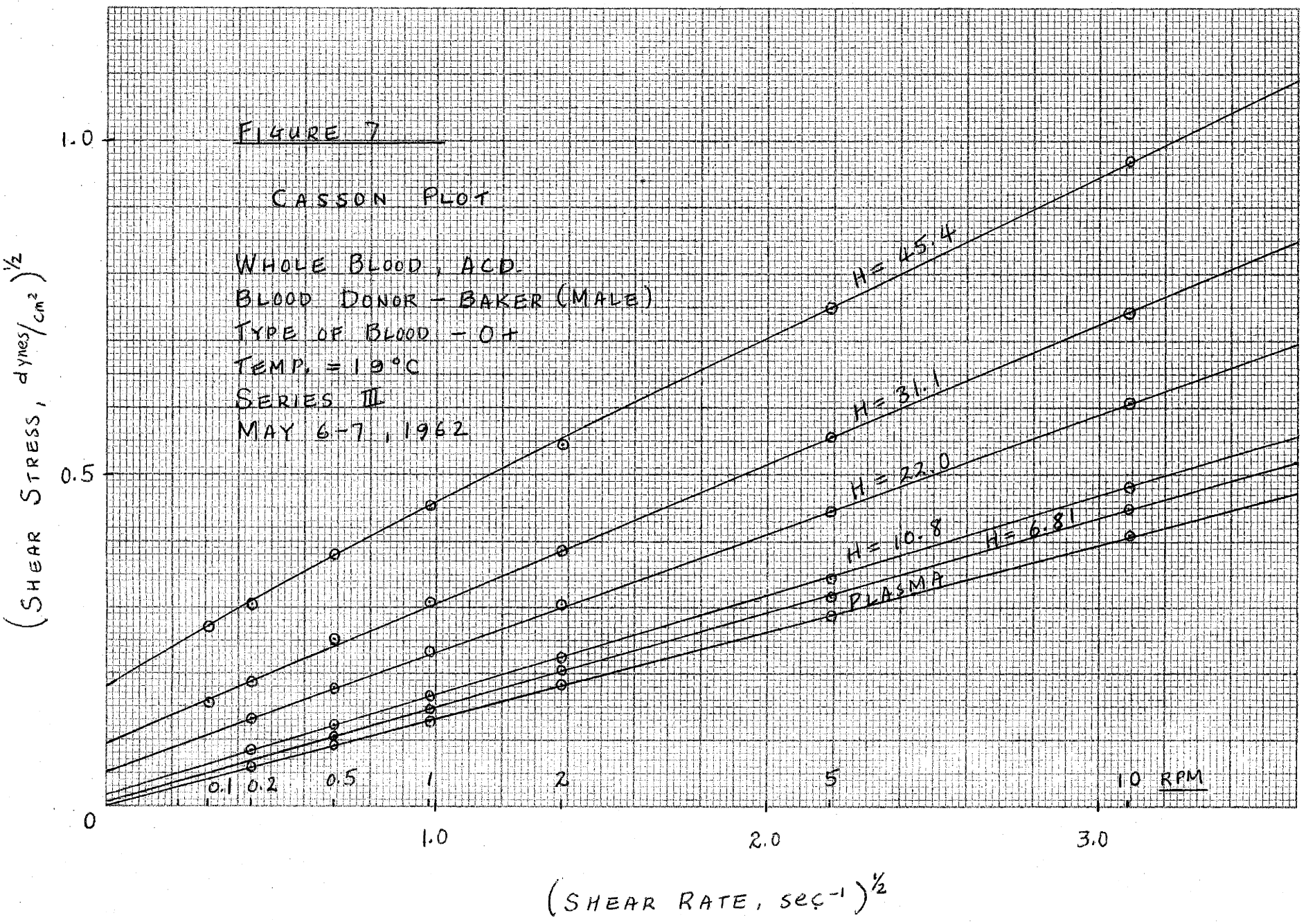


FIGURE 7
CASSON PLOT
WHOLE BLOOD, ACD.
BLOOD DONOR - BAKER (MALE)
TYPE OF BLOOD - O+
TEMP. = 19°C
SERIES III
MAY 6-7, 1962
H = 45.4
H = 31.1
H = 22.0
H = 10.8
H = 6.81
PLASMA
1.0
0.5
0
0.1
0.2
0.5
1
2
5
10 RPM
1.0
2.0
3.0
(SHEAR STRESS, dynes/cm²)^½
(SHEAR RATE, sec⁻¹)^½

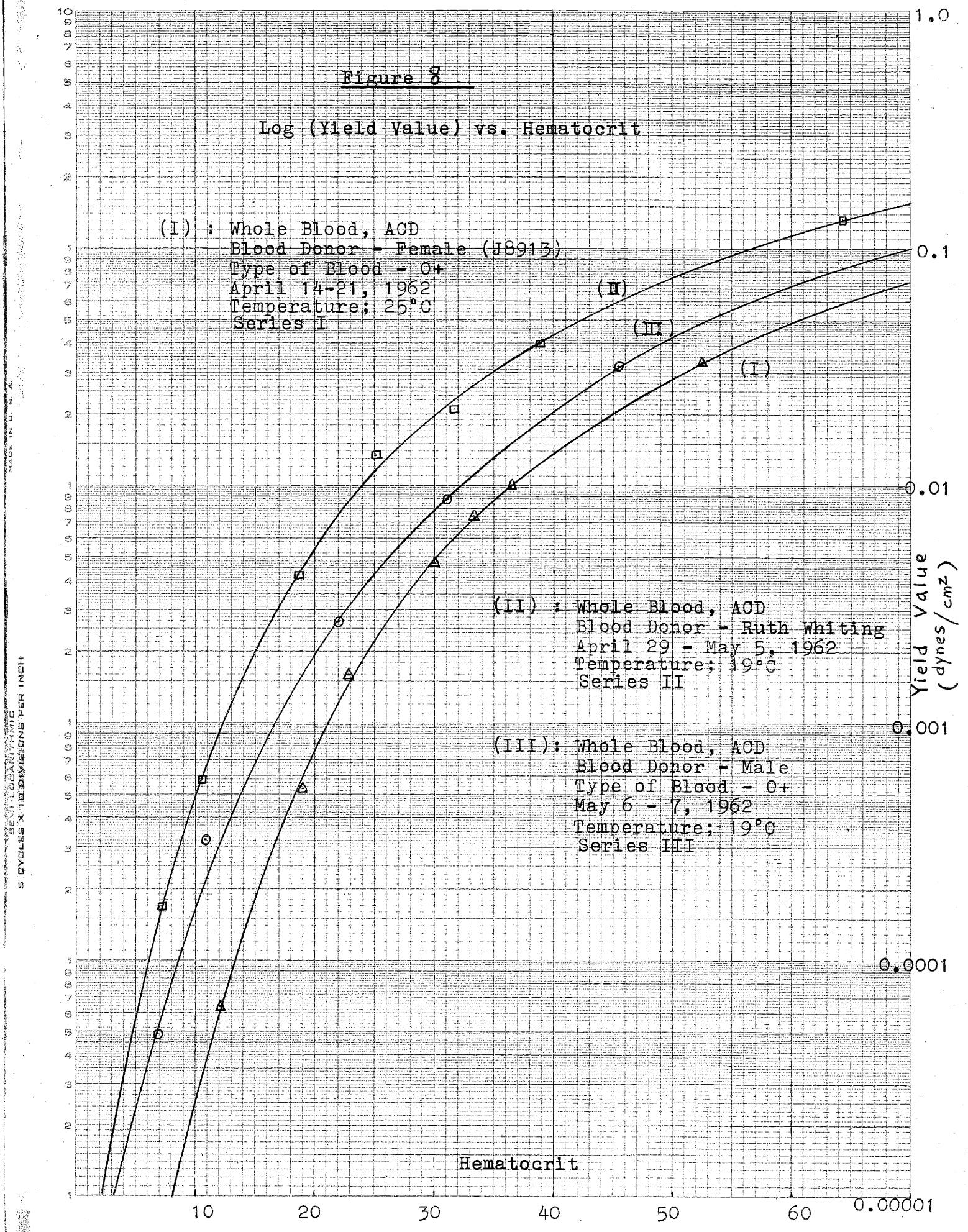


Figure 8
Log (Yield Value) vs. Hematocrit
(I) : Whole Blood, ACD
Blood Donor - Female (J8913)
Type of Blood - O+
April 14-21, 1962
Temperature; 25°C
Series I
(II) : Whole Blood, ACD
Blood Donor - Ruth Whiting
April 29 - May 5, 1962
Temperature; 19°C
Series II
(III): Whole Blood, ACD
Blood Donor - Male
Type of Blood - O+
May 6 - 7, 1962
Temperature; 19°C
Series III
(I)
(II)
(III)
Yield Value (dynes/cm²)
1.0
0.1
0.01
0.001
0.0001
0.00001
Hematocrit
10
20
30
40
50
60

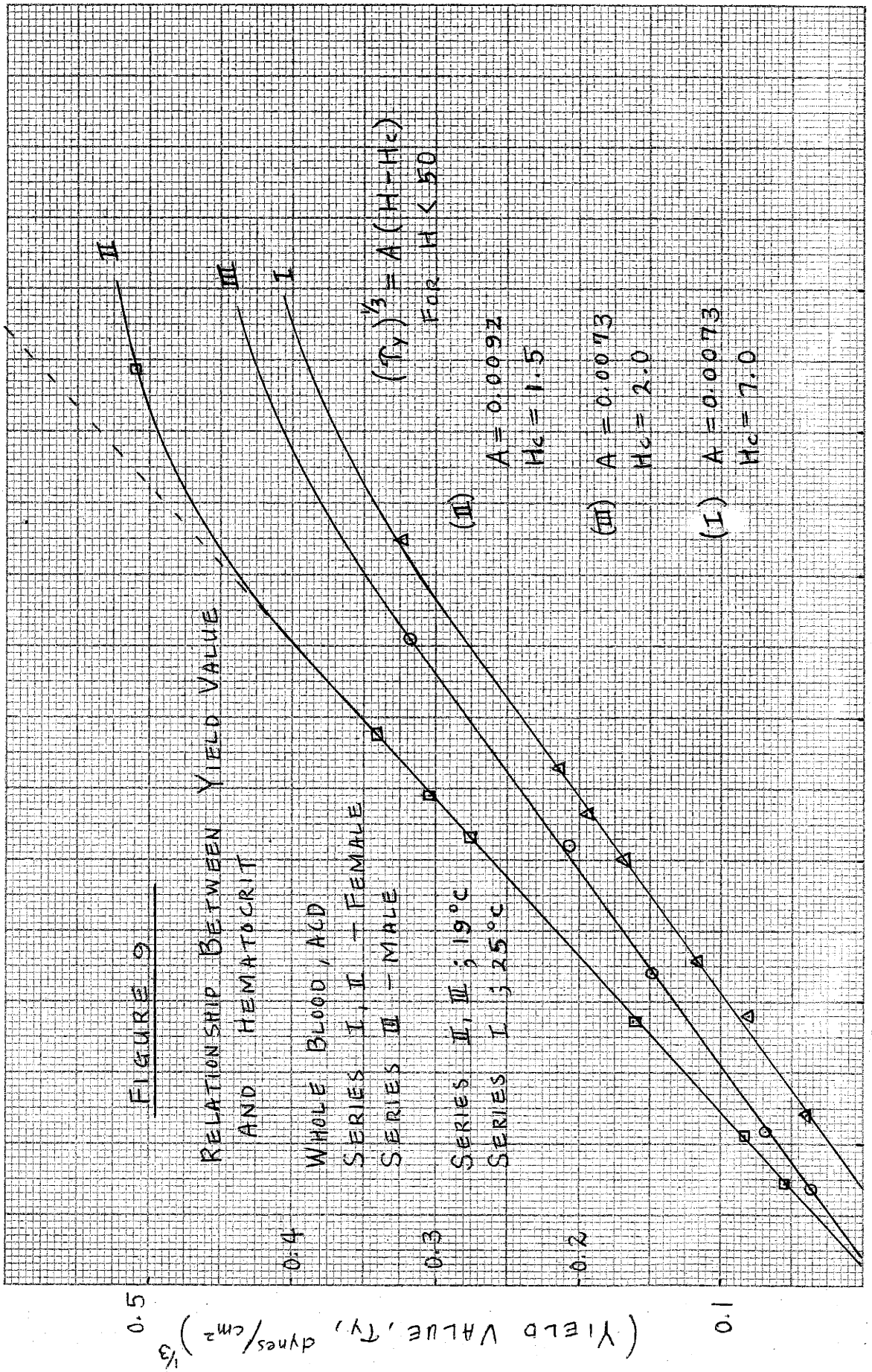


FIGURE 9
RELATIONSHIP BETWEEN YIELD VALUE AND HEMATOCRIT
WHOLE BLOOD, AGD
SERIES I, II - FEMALE
SERIES III - MALE
SERIES II, III ; 19°C
SERIES I ; 25°C
$(\tau_y)^{1/3} = A(H-H_c)$
FOR $H < 50$
(II) $A = 0.0092$
$H_c = 1.5$
(III) $A = 0.0073$
$H_c = 2.0$
(I) $A = 0.0073$
$H_c = 7.0$
I
II
III
0.5
0.4
0.3
0.2
0.1
10
20
30
40
50
60
70
(Yield Value, τ_y, dynes/cm^2)$^{1/3}$
HEMATOCRIT

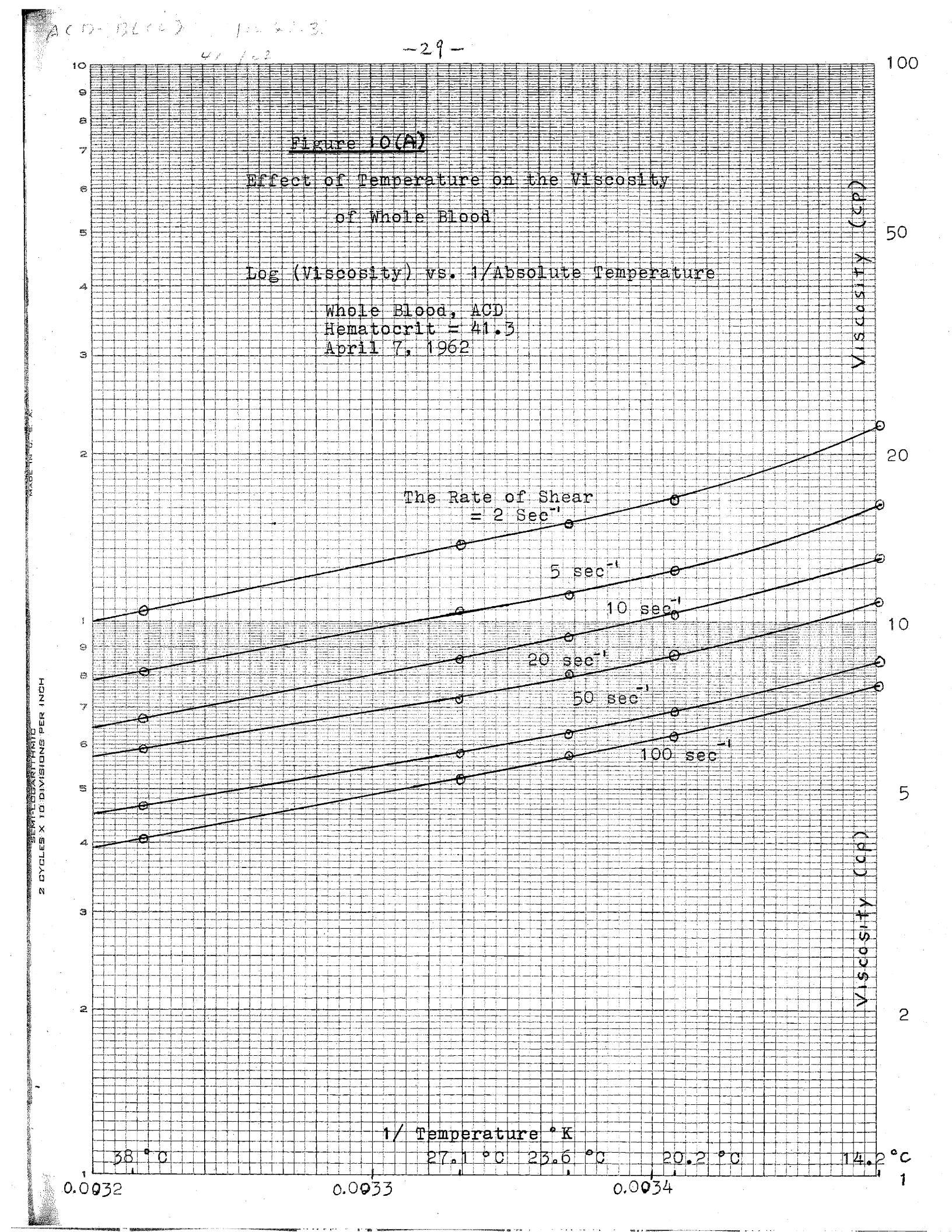


Figure 10(A)
Effect of Temperature on the Viscosity of Whole Blood
Log (Viscosity) vs. 1/Absolute Temperature
Whole Blood, ACD
Hematocrit = 41.3
April 7, 1962
The Rate of Shear = 2 Sec⁻¹
5 sec⁻¹
10 sec⁻¹
20 sec⁻¹
50 sec⁻¹
100 sec⁻¹
Viscosity (cp)
Viscosity (cp)
1/ Temperature °K
38 °C
27.1 °C
23.6 °C
20.2 °C
14.2 °C
0.0032
0.0033
0.0034
SEMI-LOGARITHMIC
2 CYCLES X 10 DIVISIONS PER INCH

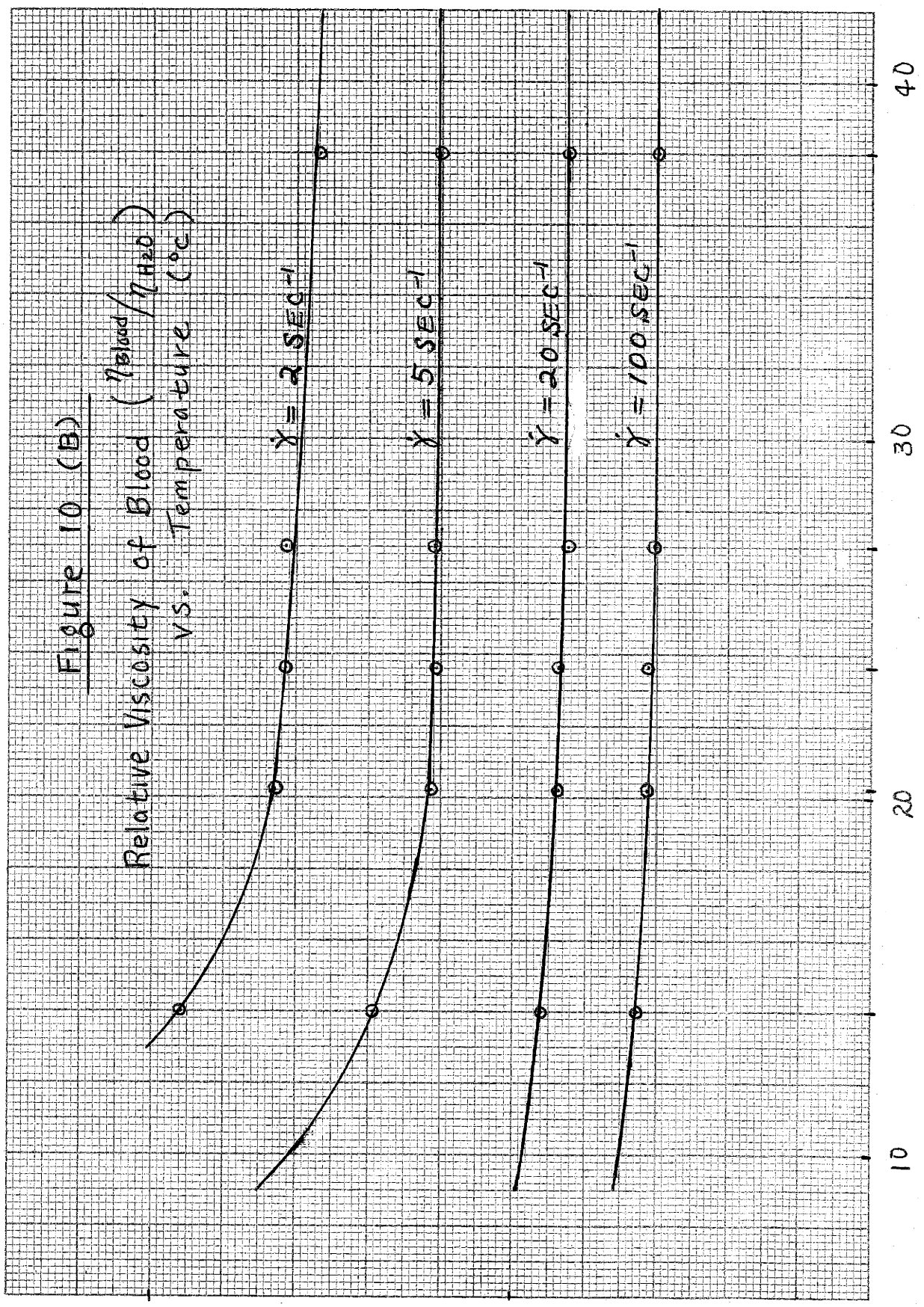


Figure 10 (B)
Relative Viscosity of Blood (η_{blood}/η_{H_2O}) vs. Temperature (°C)
$\dot{\gamma} = 2\ sec^{-1}$
$\dot{\gamma} = 5\ sec^{-1}$
$\dot{\gamma} = 20\ sec^{-1}$
$\dot{\gamma} = 100\ sec^{-1}$
$\frac{\eta_{blood}}{\eta_{H_2O}}$
20
0
10
20
30
40
Temperature (°C)

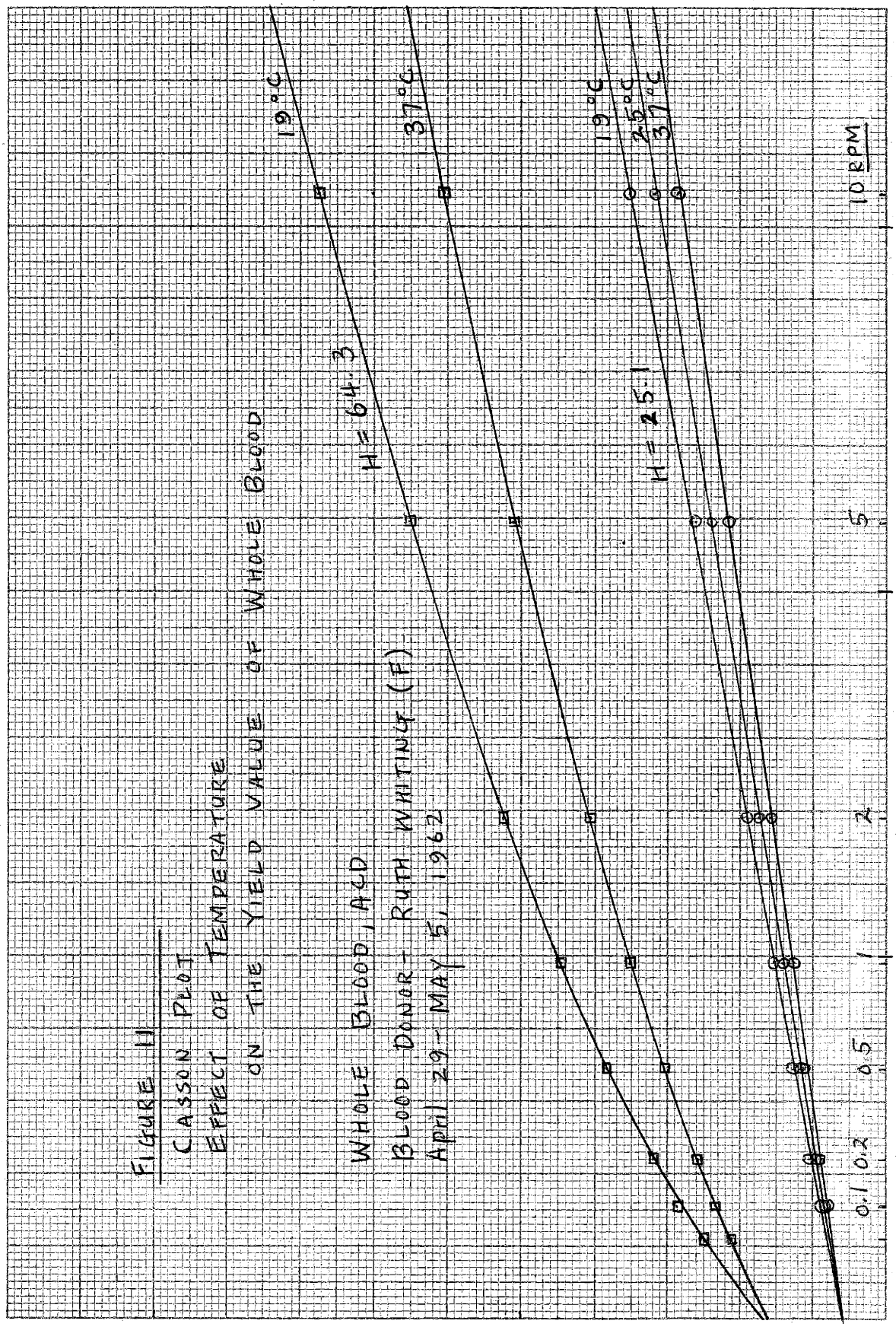


FIGURE II

CASSON PLOT

EFFECT OF TEMPERATURE

ON THE YIELD VALUE OF WHOLE BLOOD

WHOLE BLOOD, ACD

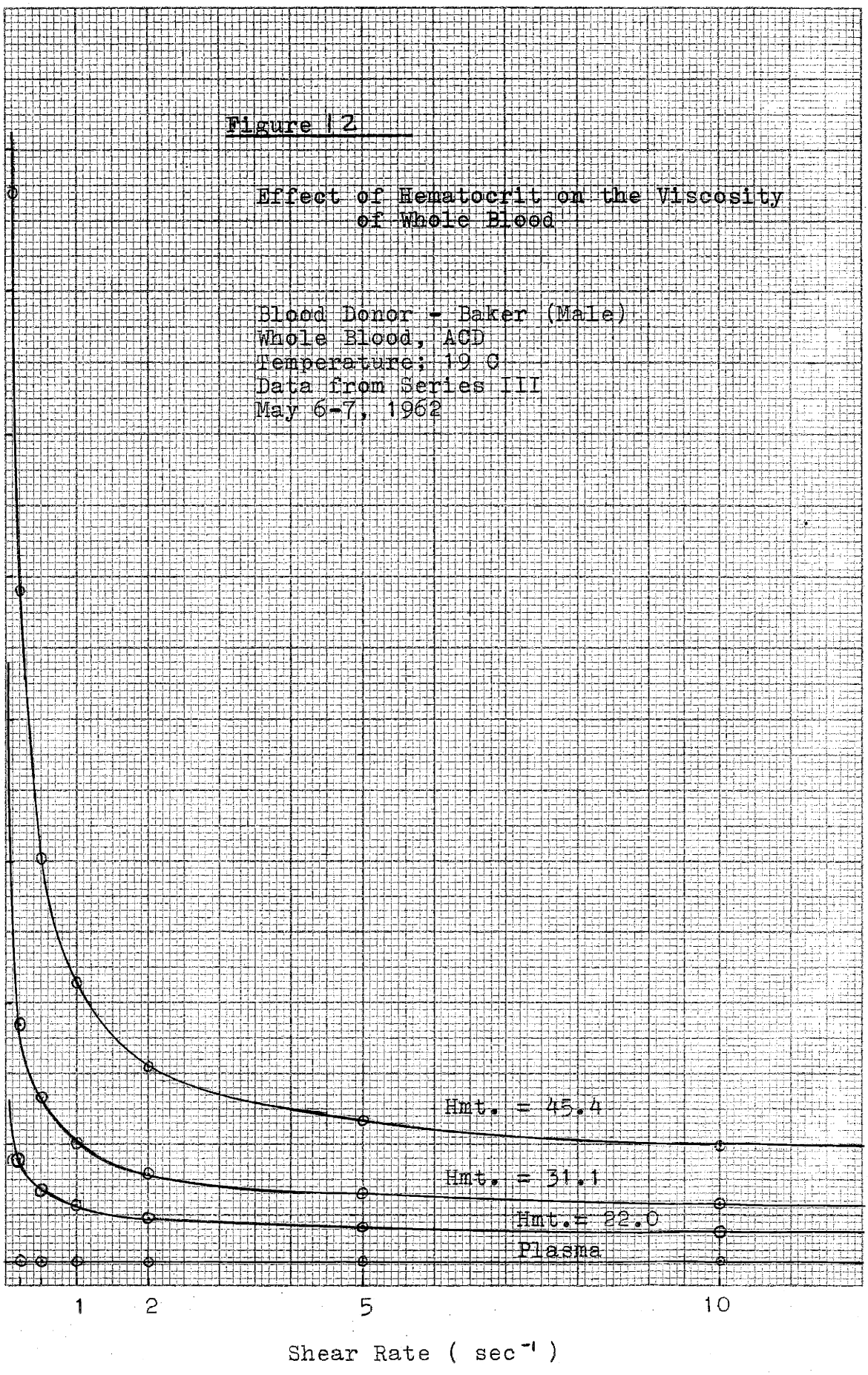
BLOOD DONOR - RUTH WHITING (F)

April 29 - MAY 5, 1962

Figure 12

Effect of Hematocrit on the Viscosity of Whole Blood

Blood Donor - Baker (Male)
Whole Blood, ACD
Temperature: 19 C
Data from Series III
May 6-7, 1962



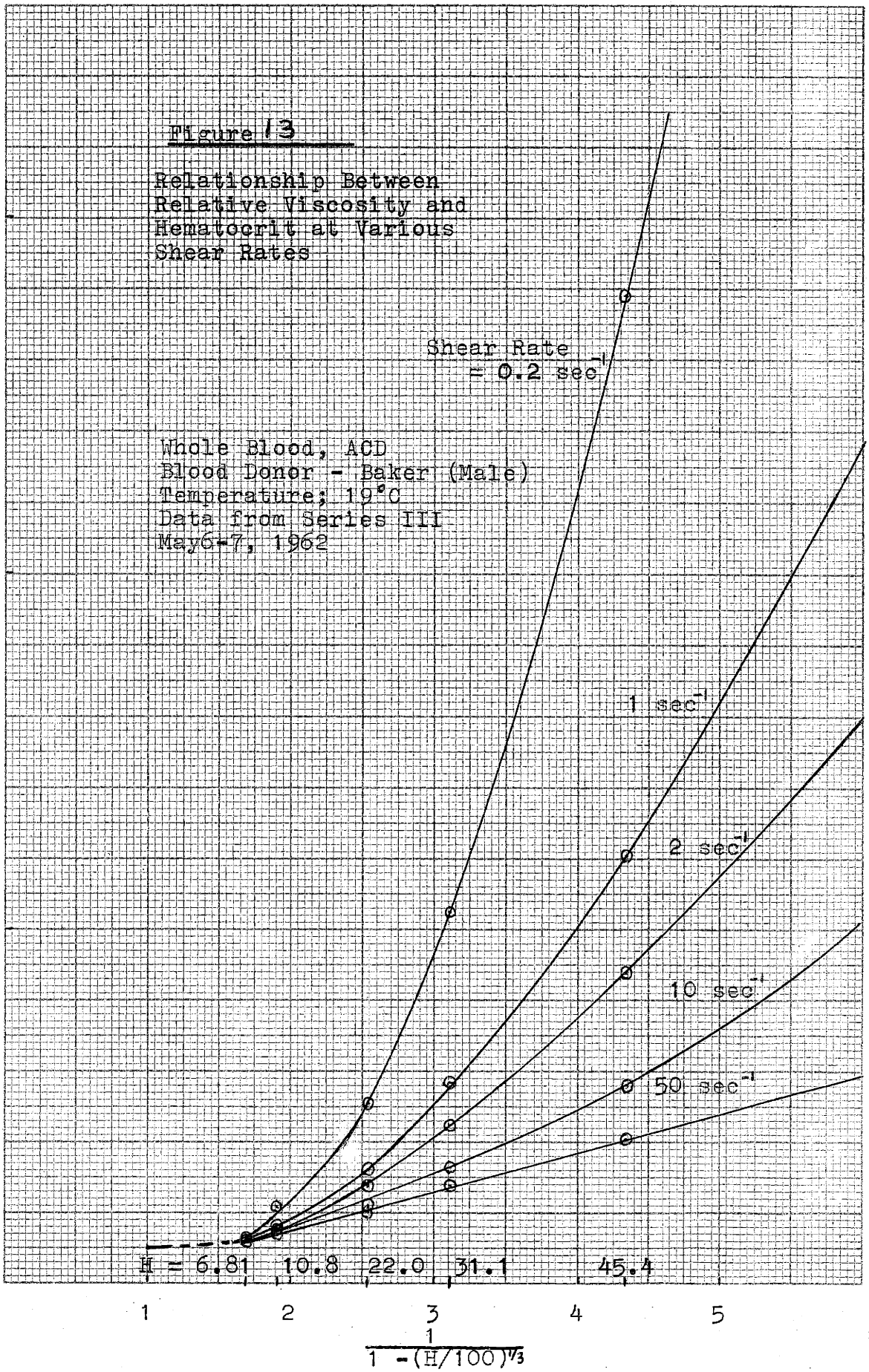


Figure 13
Relationship Between Relative Viscosity and Hematocrit at Various Shear Rates
Shear Rate ≈ 0.2 sec⁻¹
Whole Blood, ACD
Blood Donor - Baker (Male)
Temperature; 19°C
Data from Series III
May6-7, 1962
1 sec⁻¹
2 sec⁻¹
10 sec⁻¹
50 sec⁻¹
H = 6.81 10.8 22.0 31.1 45.4
Relative Viscosity (η/ηp)
0
10
20
30
1
2
3
4
5
1 / 1 - (H/100)^1/3

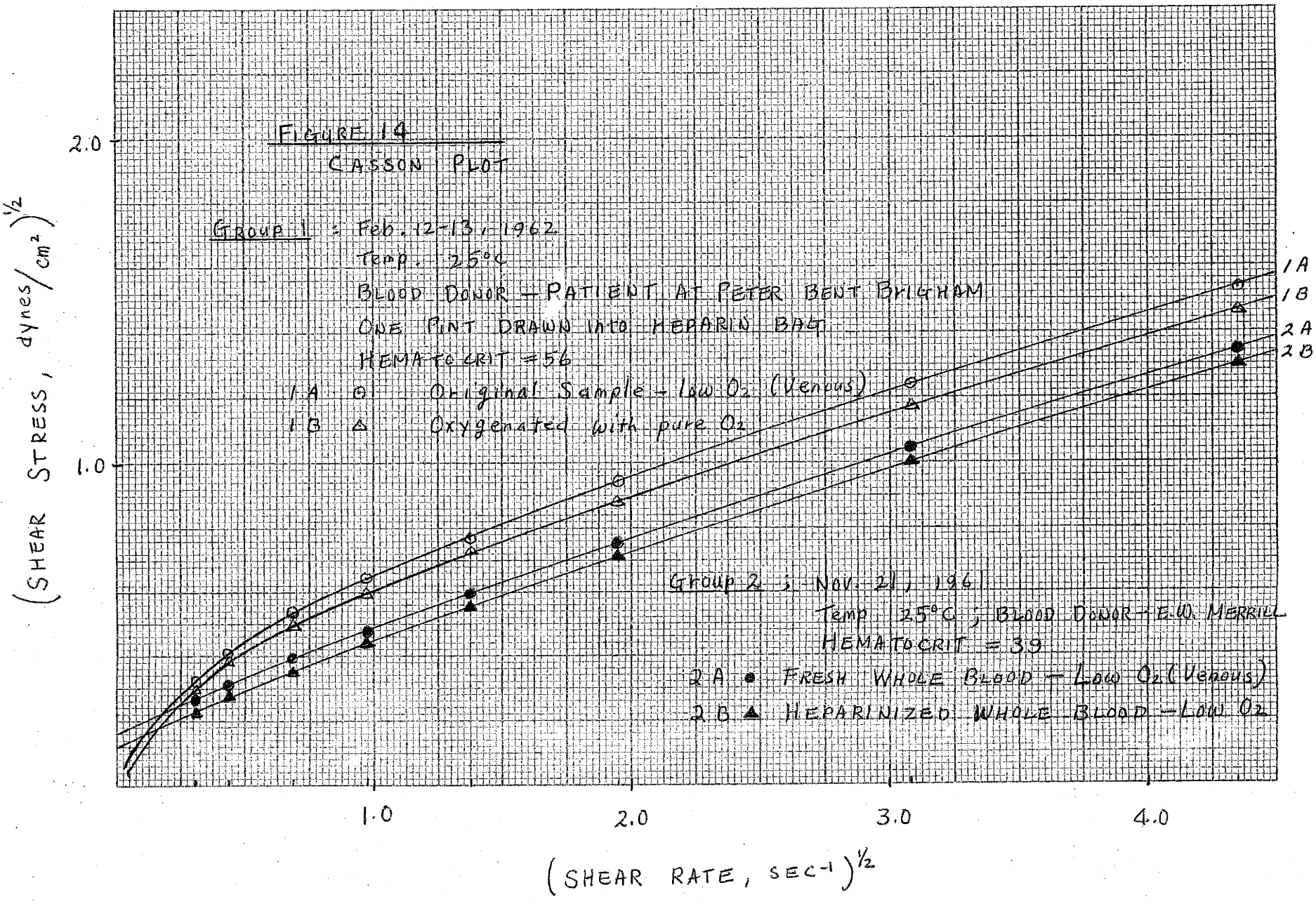
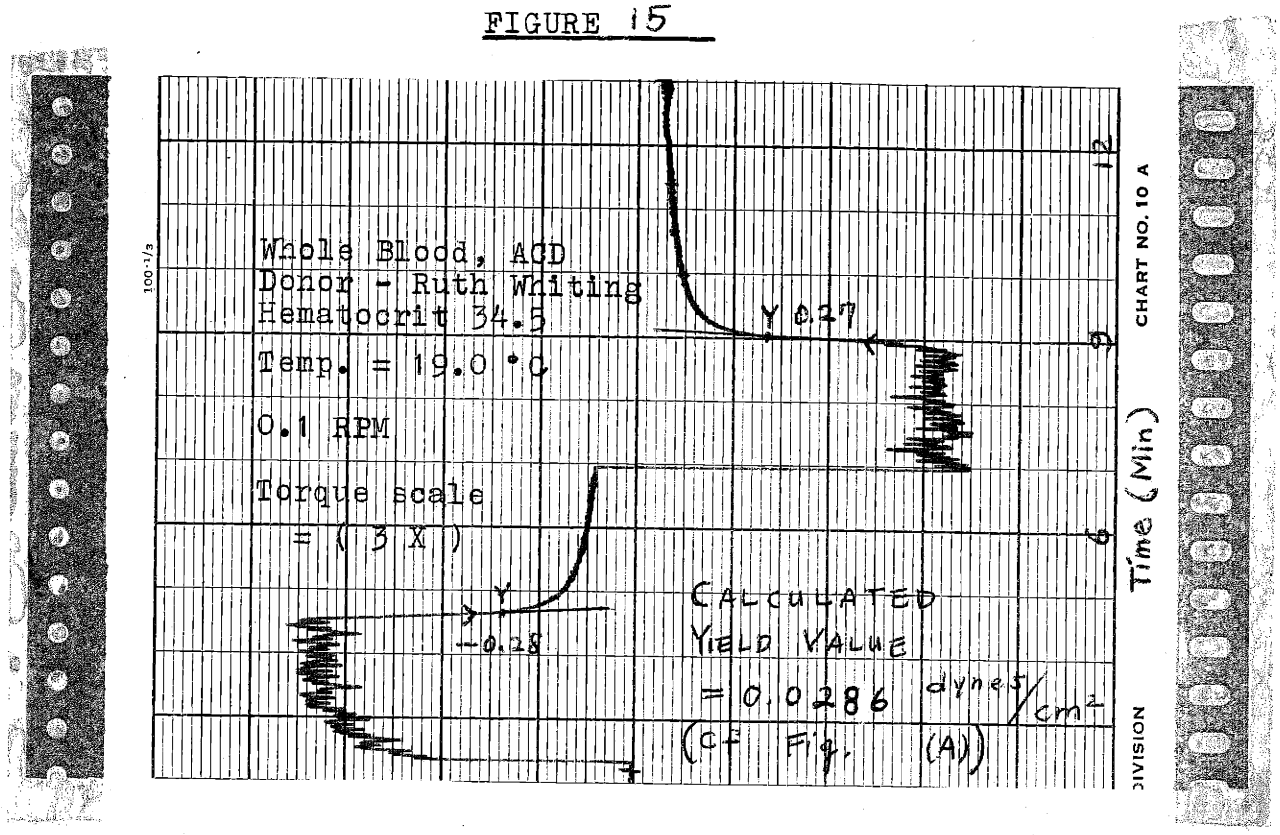
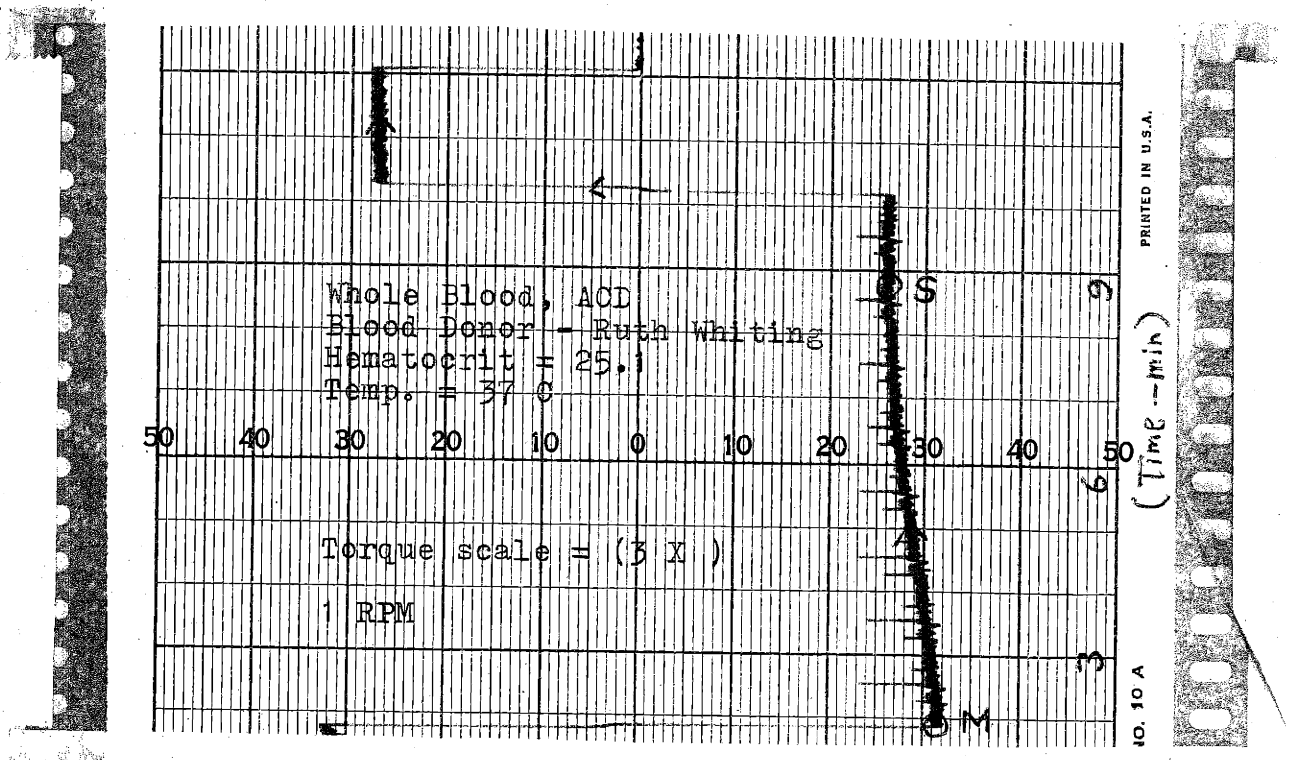


FIGURE 14
CASSON PLOT
GROUP 1 : Feb. 12-13, 1962
Temp. 25°C
BLOOD DONOR — PATIENT AT PETER BENT BRIGHAM
ONE PINT DRAWN INTO HEPARIN BAG
HEMATOCRIT = 56
1A ○ Original Sample — low O2 (Venous)
1B △ Oxygenated with pure O2
GROUP 2 : NOV. 21, 1961
Temp 25°C ; BLOOD DONOR — E.W. MERRILL
HEMATOCRIT = 39
2A ● FRESH WHOLE BLOOD — LOW O2 (Venous)
2B ▲ HEPARINIZED WHOLE BLOOD — LOW O2
1A
1B
2A
2B
2.0
1.0
1.0
2.0
3.0
4.0
(SHEAR STRESS, dynes/cm²)^1/2
(SHEAR RATE, sec⁻¹)^1/2

FIGURE 15


Whole Blood, ACD
Donor - Ruth Whiting
Hematocrit 34.5
Temp. = 19.0 °C
0.1 RPM
Torque scale
= (3 X)
Y 0.27
Y
-0.28
CALCULATED
YIELD VALUE
= 0.0286 dynes/cm²
(cf Fig. (A))
Time (Min)
CHART NO. 10 A

(A)


Whole Blood, ACD
Blood Donor - Ruth Whiting
Hematocrit = 25.1
Temp. = 37 C
50 40 30 20 10 0 10 20 30 40 50
Torque scale = (3 X)
1 RPM
(Time - min)
PRINTED IN U.S.A.

(B)

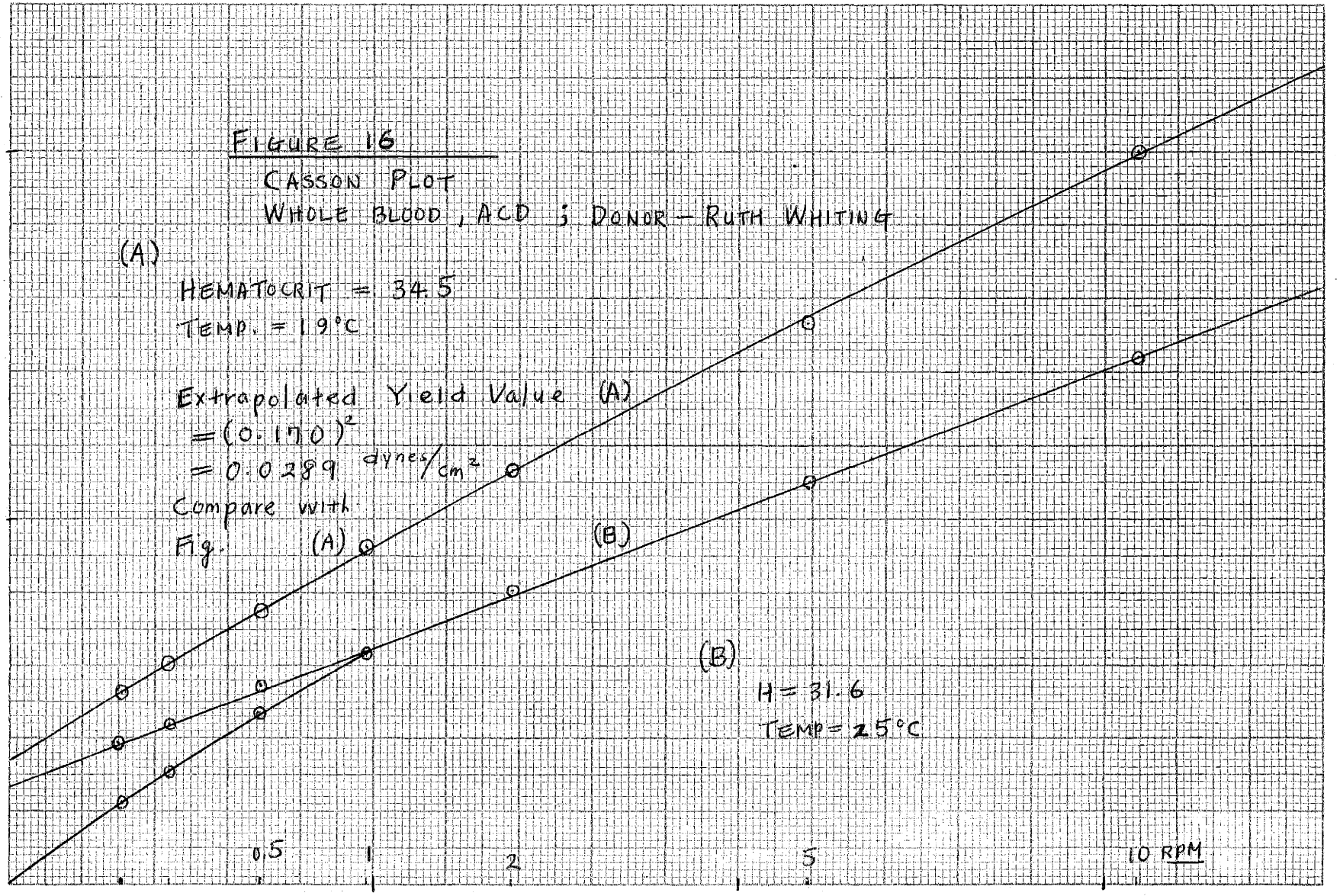


FIGURE 16
CASSON PLOT
WHOLE BLOOD, ACD; DONOR – RUTH WHITING
(A)
HEMATOCRIT = 34.5
TEMP. = 19°C
Extrapolated Yield Value (A)
= (0.170)²
= 0.0289 dynes/cm²
Compare with
Fig. (A)
(B)
(B)
H = 31.6
TEMP = 25°C
0.5
1
2
5
10 RPM
1.0
0.5
1.0
2.0
3.0
(SHEAR STRESS, dynes/cm²)^1/2
(SHEAR RATE, SEC⁻¹)^1/2

V. DISCUSSION OF RESULTS

(A) Assumption

Before discussing the experimental results, it is mandatory to mention one important assumption made.

At high shear rates (i.e., above 2 sec^{-1}) the torque reading was constant and did not change with time. But at low shear rates (below 2 sec^{-1}) the torque reading first reached a maximum value, then started to decrease, slowly approaching a certain steady value. Then the torque tended to increase again due to the sedimentation of red cells (Figure 15A).

This unusual situation certainly poses one question: Which point on the curve represents the true shear stress ? It is believed that the true shear stress is best approximated by the torque reading at the maximum point, for reasons to be discussed below.

If blood is left at rest or if blood is set into a mild laminar flow, then marginal layers of clear plasma form at the wall surfaces. Since the marginal layer has a relatively low viscosity, it is reasonable to regard it as allowing the main body of the stream to "slip" at the wall. This "slippage" at the wall appears to be responsible

for the initial decrease of the torque reading. As time passes, an additional mechanism sets in which also reduces the torque reading. This mechanism is the orientation of rod-like red cell aggregates (rouleaux) along the fluid stream lines.

The formation of marginal plasma layers is well known in studies of capillary circulation (19a, 20, 7, 8). When blood flows through narrow tubes, the red cells tend to accumulate along the axis, leaving a plasmatic zone near the walls. This situation can be clearly seen in motion pictures of circulation in small vessels. Taylor believes that the marginal plasma layer effects are negligibly small in large vessels, but are appreciably large in small vessels. (19)a. Since the gap between the two cylinders in the G.D.M. Viscometer is only about 1.5 mm wide, it is reasonable to assume that the presence of a plasma layer should reduce the torque reading. Reiner derived a theoretical expression for correcting for wall effects (21).

The orientation effects under shear were also studied by several workers (22, 1, 23). It is generally agreed that such an orientation generally reduces the viscosity of suspensions.

If we assume that the marginal layer actually forms and that the formation of such a layer gives an erroneous

torque reading, then it is imperative to find some method by which a true shear stress can be obtained. Our usual procedure for this consisted of 1) stirring up the fluid well before taking a reading for each shear rate, 2) then of taking the maximum point on the torque-time curve from an automatic torque recorder. All experimental data on shear stress presented in this report are calculated from such maximum torque readings.

The maximum value M and the minimum (or steady state) value S are both plotted on a Casson plot in Figure 16B. It can be seen from the plot that the maximum points fit the Casson plot remarkably well, whereas the minimum points bend downward towards the origin.

As was mentioned already in the Introduction, Casson's equation was derived for a suspension of long, rigid flocculates. This Casson's model resembles the rheological structure of blood. (See Discussion B). The fact that the maximum points fit the Casson model seems to be an indication that the use of the maximum points of the torque-time curves is essentially correct.

(B) Yield Value and the Rheological Structure of Blood

Red cells in blood of a healthy person tend to unite with

their flat sides against each other forming a rod-like aggregates called rouleaux (29). If blood is left at rest, rouleaux tend to join one another to form a continuous network. This network gives blood a rigid structure which is responsible for its plasticity and its yield value.

At very low shear rates the network tends to break up and then to build up again, thus finally reaching a dynamic equilibrium. As shear rate increases, the network, at some stage, breaks up completly and individual rouleaux line up along the fluid stream lines. As shear rate increases still further, the rouleaux disintegrate into individual red cells.

Therefore, at low shear rates the basic flow units are essentially rouleaux rather than individual red cells. But at high shear rates red cells are the basic flow units.

It is believed that the main attractive forces between the red cells are the surface tension of plasma, while the main repulsive forces are the electric forces at the double layer.

(C) Effect of Hematocrit on Yield Value

The experimental results on the effect of hematocrit on the yield value of blood were summarized in the equations

(8), (9), and (10). It was found that clay suspensions satisfied similar equations (17, 27). The critical hematocrits for the whole blood tested in the second and in the third series were 1.5 and 2.0% respectively. These two values are considerably lower than the value found for the blood of the first series (7.0%). The reason for this seems to be the following: A comparison of the $\sqrt{\tau}$ versus $\sqrt{\delta}$ curves of plasma in the three series reveals that the viscosity of plasma in the second and in the third series were approximately the same and are greater than the viscosity of plasma in the first series. This seems to indicate that the relatively lower yield values and also the relatively higher critical hematocrit for the blood in the first series were related to the lower viscosity of the plasma. Since the plasma viscosity differences are indications of differing plasma compositions, it is likely that the yield value and critical hematocrit differences arise due to differences in the plasma compositions, such as concentration variations of plasma proteins, calcium ions, etc..

Plasma composition, then, seems to be the substance that determines the magnitude of the yield value. If this is the case, a question arises as to what part of plasma allows blood to form a rigid structure which is responsible for its yield value.

Our experiments showed that red cell suspensions in albumin solutions had no yield value. Red cell suspensions in globulin solutions was also found to have no yield value, or only a very small yield value as long as the protein concentration was equal to (or less than) that found in human blood. Fähraeus oberved that red cells had the greatest tendency to aggregate in fibrinogen solution (29, 28).

It then seems most probable that fibrinogen is the constituent responsible for the yield value in blood.

This undoubtedly explain why Haynes and Burton (9) could not observe any yield value for red cell suspensions in ACD (acid-citrate-dextrose solution).

As already mentioned, equation (7) was found to be valid only when the hemotocrit was below about 50%. Above 50%, it was found that the yield value and hematocrit could be best correlated by the equation

$$\tau_y = A\, e^{BH} \qquad (11)$$

where A and B are constants. Green (24, 25) found that many pigment-oil suspensions satisfy this equation at high concentrations of pigment.

The occurance of a critical concentration for yield value is quite common for many suspensions (15). For in-

stance, Schofield and Scott Blair found that a yield value could be observed at a volume concentration as low as 2 % for a clay suspension (26). Bolger obtained similiar results (17). This critical concentration for clay suspensions is approximately the same in magnitude as the critical hematocrits found for blood.

(D) Effect of Temperature on Yield Value

The experimental results show that the yield value is independent of temperature for blood samples having a hematocrit below 30%, but it increases slightly with decreasing temperature for blood samples above 30%.

If the logarithm of yield values taken at three different temperatures are plotted against hematocrits, curves like that shown in Figure 17 will result.

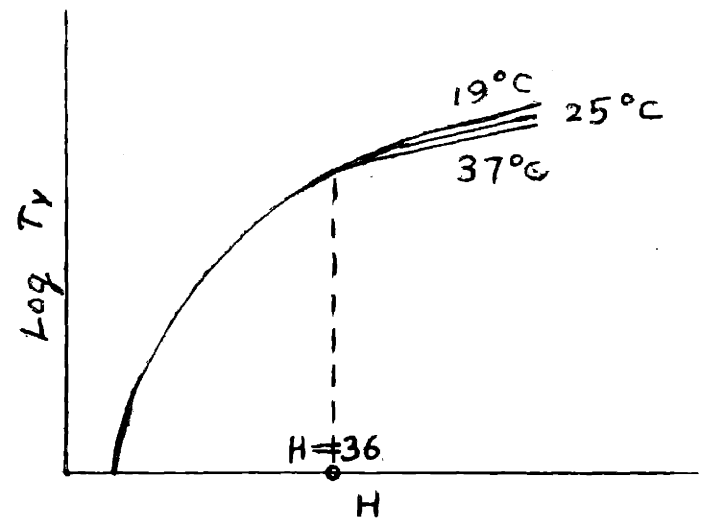


Fig. 17 Log τ_y vs. Hematocrit at different temperature.

(E) An Alternative Method for Obtaining a Yield Value

Figures 15(A) and 16(A) were meant to illustrate two different methods for obtaining yield value.

The former shows how the torque reading decades with time when shear stress is released. Initially the viscometer bob was rotating counterclockwise at 0.1 RPM. As the motor was turned off, the torque reading dropped rapidly to a certain point, then started to decay exponentially with time. A similar result was observed when the bob initially was rotated clockwise.

The shear stress corresponding to the torque at the point Y in Figure 15(A) was found to be approximately the same as the yield value obtained from the Casson plot (Figure 16A); Y is the point at which the torque-time curve changes its slope sharply.

It is believed that the initial rapid drop in the torque reading is due to the relaxation of the fluid blood and that the slow exponential decay is due to the elastic deformation of the pseudosolid blood. Then, the point Y should represent the torque reading which corresponds to the yield value.

Unfortunately it was not very easy to determine at exactly which point the torque-time curve changed its slope

Because of this difficulty, several trials, made to obtain the yield value, gave slightly different values for an identical sample.

(F) Additional Variables

Among the many variables that affect the rheological properties of blood, only hematocrit, temperature and shear rate were considered.

Some other variables include: the kind and the amount of anticoagulants used to prevent clotting, the composition of the plasma, the type of red cells, various diseases of the blood donor, the size of the cup and the bob of the viscometer, and PH.

It was found that the effect of anticoagulants was very small, if existent at all. Consequently, it could not have affected our experimental results to any appreciable degree. The measurement of PH for blood samples indicated that PH was practically constant and was in the range between 7.0 and 7.5. Hence, its influence should also be negligible.

The other variables mentioned were, however, uncontrollable during the present investigation. Their effects on the rheological properties of blood were left for future study.

VI. CONCLUSIONS

Whole blood was found to possess yield values. The critical hematocrit for the yield value first to appear was 2% or slightly higher depending on the plasma compositions. It was also found that the yield value increased very rapidly with increasing hematocrit.

Below hematocrit of about 50%, the yield value and hematocrit could be best correlated by the equation

$$\tau_y^{1/3} = A\,(H - H_c) \qquad (7)$$

and above 50%, by the equation

$$\tau_y = D\,e^{BH} . \qquad (11)$$

The yield value appeared to be independent of temperature for blood samples having an hematocrit below 30%. Above 30%, the yield value seemed to increase with decreasing temperature by a very small amount.

The apparent viscosity of blood was found to increase rapidly as temperature fell. However, the relative viscosity of blood, which is defined as the ratio of the viscosity of blood at any temperature to the viscosity of water at the same temperature, did not change very much with temperature above 20 °C. Below 20 °C the relative viscosity began to increase appreciably as temperature decreased.

VII. RECOMMENDATIONS

1. Fibrinogen is believed to be responsible for the yield value of blood. A study on the rheological properties of the red cell suspensions in the fibrinogen solution is to be carried out in order to prove this hypothesis.

2. Copley claimed that the larger the amount of heparin used, the lower the viscosity of blood becomes (6). Many physiologists believe that other anticoagulants have similar effects on the viscosity. A systematic study on the effects of various anticoagulants on the rheological properties of blood is recommended.

3. The relaxation method for obtaining the yield value of blood was not very accurate due to the difficulty of locating the point at which the torque-time curve changes its slope. A modification on the instrument may improve its accuracy.

4. An effort was made for the systematic investigation of the effect of temperature on the yield value of blood throughout the range of hematocrits from 7.2 to 64.3 . Unfortunately some of the obtained data for this study were not reliable due to the temporary failure of the air-bearing. More investigation on the subject, especially for blood samples of hematocrits between 30% and 50%, is recommended.

VIII. APPENDIX

(A) G.D.M. Viscometer

The G.D.M. viscometer employed in this investigation was named after those who was responsible for its development, namely, Mr. P. Gilinson, Mr. C.R. Dauwalter, and Professor E.W. Merrill.

The viscometer part of the instrument consists essentially of two concentric cylinders (Figure 18).

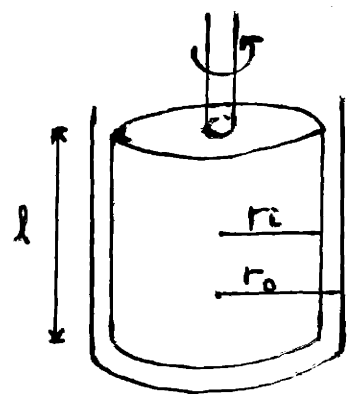


Figure 18 Couette viscometer

As the inner cylinder rotates, fluid sample in the annular gap exerts torque to the outer cylinder. This torque is then measured by the torque-to-balance loop (See VIII APPENDIX B).

It can be shown that, for a Newtonian liquid, shear stress and shear rate are related to torque and the rotational

speed of the inner cylinder respectively by the following equations :

$$\tau = \frac{T}{2\pi r_o^2 l} \qquad (12)$$

$$\dot{\gamma} = \frac{2r_o^2 \omega}{r_o^2 - r_i^2} = \frac{2r_o^2}{r_o^2 - r_i^2} \left(\frac{2\pi N}{60} \right) \qquad (13)$$

where T = torque (dyne-cm)

r_o = radius of outer cylinder

r_i = radius of inner cylinder

l = height of annular gap

and N = revolutions per minute of inner cylinder (RPM) .

Dimensions for the two cylinders of the viscometer used in this investigation were

r_o = 0.4951 inches

r_i = 0.4375 "

and l = 1.1400 " .

Hence, equations (12) and (13) can be written

$$\tau \text{ (dyne/cm}^2\text{)} = \frac{T \text{ (dyne-cm)}}{28.77} \qquad (12)'$$

$$\dot{\gamma} \text{ (sec}^{-1}\text{)} = 0.9557 \text{ N (RPM)} \quad . \qquad (13)'$$

Above equations can be used as a good approximation for

non-Newtonian liquids provided that the annular gap is small compared to r_o or r_i.

In deriving these equations, it was assumed that there was no slippage at the wall. The range of shear rate of the G.D.M. viscometer is from 0.02 sec^{-1} to 100 sec^{-1}.

(B) An A-C Torque-to-Balance Measuring System (30)

The a-c torque-to-balance measuring system is a closed loop measuring system that has been developed to accurately determine low levels of torque. A simplified schematic diagram of the system is shown in Figure 19.

As the external torque T is applied to the torque-summing member shaft, the shaft begins to rotate through an angle θ and an angular displacement signal voltage developes at the secondary winding of the signal generator. This voltage is amplified by a power amplifier that feeds back a current to develope a counter or balancing torque in the torque generator. This torque is transferred to a product resolver. This transient action continues until torque equilibrium on the torque summing member shaft is reached. Then, the d.c. current reading from the microammeter, when the equilibrium is reached, is a measure of the external torque applied to the shaft.

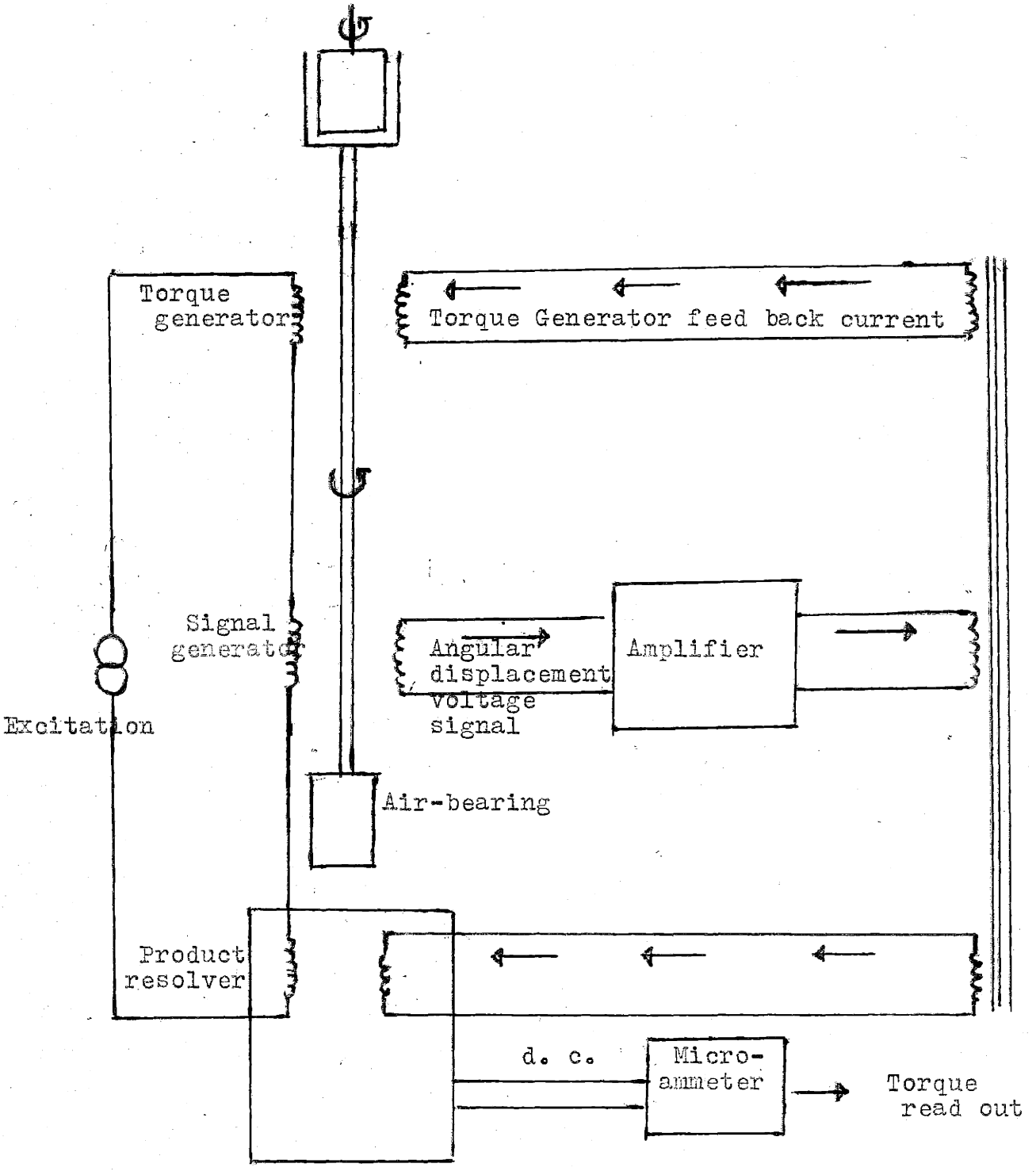


Figure 19 Simplified schematic of the a-c torque-to-balance measuring system

(C) Typical Data and Sample Calculations

RPM	Torque ccw	Torque cw	Actual Torque
100	-300•0.590	300•0.59	177.0
50	-200.0.490	200•0.49	98.0
20	-100•0.465	100•0.46	46.25
10	- 60•0.455	60•0.45	27.15
5	- 30•0.540	30•0.54	16.2
2	- 20•0.435	20•0.42	8.55
1	- 10•0.585	10•0.595	5.90
0.5	- 8•0.510	8•0.53	4.16
0.2	- 6•0.450	6•0.45	2.70
0.1	- 4•0.530	4•0.53	2.12

TABLE 4 TYPICAL DATA

T = 27.15 dynes-cm at 10 RPM.

i) $\dot{\gamma} = \frac{2r_o^2(2\pi N)}{(r_o^2 - r_i^2)\,60} = 0.956\ N = 0.956 \cdot 10$

$= 9.56\ \text{sec}^{-1}$

ii) $\tau = \frac{T}{2\pi r_o^2 l} = \frac{T}{28.8} = \frac{27.15}{28.80} = 0.942\ \text{dynes/cm}^2$

iii) $\eta = \frac{\tau}{\dot{\gamma}} = \frac{0.942}{9.560} = 0.0988$ poises or 9.88 centipoises

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