SLUDGED BLOOD

BY *MILTON L. ZISOWITZ*

BLOOD is synonymous with life. When it stops flowing through the thousands of miles of arteries, veins and capillaries which reach out into the remotest parts of the body, death follows quickly. Everyone knows this. Few people know, however, that there are times — in disease, in injury, in old age — when the blood begins to lose its liquid character, to clump together into masses, to plug some of the smaller vessels. When this happens, even though the general circulation may continue seemingly unimpeded, parts of the organism are deprived of the oxygen and other nutrients they need to carry on their functions, and damage — even death — may be the result. This "sludging" of the blood has been observed for almost a century, but not until comparatively recent times have scientists begun to study the phenomenon systematically. Only a few months ago, the first comprehensive reports on sixteen years of intensive research began to come from the laboratories of Drs. Melvin H. Knisely, Edward H. Bloch, Theodore S. Eliot, and Louise Warner, of the Universities of Chicago, Copenhagen, and Tennessee. And, though the reports were cautious, they have created an unusual stir among physicians and biologists. For in addition to opening up entirely new fields in the investigation of blood disease, the experiments that Dr. Knisely and his associates are conducting may furnish important clues toward the solution of one of the oldest and most baffling of medical problems — the problem of aging.

Although it has been studied almost from the beginning of medical history, blood has not yet revealed all its secrets to the scientists. Every bright schoolboy knows the basic facts: that the seemingly homogeneous liquid really consists of red and white cells floating in a straw-colored plasma; that the red cells pick up oxygen as they pass through the lungs and deliver it to all parts of the body; that the white cells engulf and destroy invading organisms; that the bloodstream not only carries nutrients to all the tissues, but also removes waste

MILTON L. ZISOWITZ *is a teacher of English in the New York City high schools and a writer on scientific subjects for the* MERCURY *and other magazines. Together with Eleanor Bennett he contributed "New Facts about Pernicious Anemia" to these pages in February. This report has been checked and approved by several specialists in the field.*

products from the system; that the flow of this essential fluid to every cell of the body through a complex closed pipeline of arteries, capillaries, and veins is kept in ceaseless motion by the pumping action of the heart. But the blood has many other components and many additional functions, and scientists are constantly seeking and finding new ones. Some of these are fully understood, others are still being investigated. Still obscure, for example, are the functions of the platelets — the colorless, disc-like bodies which float in the plasma along with the red and white cells. Research workers are still probing the mysteries of blood pressure, especially its unaccountable fluctuations in illness and in health. Not yet satisfactorily explained, either, is the mechanism of clot formation. But despite these gaps in our knowledge, the last few years have witnessed enormous advances in knowledge concerning the special properties of blood.

II

The man who has probably done most to hasten this progress is Dr. Edwin J. Cohn, Chairman of the Department of Physical Chemistry at the Harvard Medical School. His world famous researches in blood protein fractionation have been milestones in the march of scientific knowledge, and they have saved countless lives. Concentrating his work on the plasma, Dr. Cohn has broken this straw-colored fluid into five separate fractions, four of which have already been shown to possess definite physiologic functions and therapeutic values. The largest single component of the plasma is Serum Albumin, whose function is to maintain an adequate volume of blood in the body. Unlike whole plasma, for which it is a perfect substitute in cases of shock and severe burns, Serum Albumin lasts indefinitely, needs no refrigeration even in the tropics, and does not have to be converted into powdered form for transportation or storage. Another fraction, the Gamma Globulins, carries the antibodies that help in the organism's fight against disease. The Gamma Globulins have already proved effective in the prevention and treatment of measles and jaundice, and studies of their value in other diseases such as diphtheria, whooping cough, mumps and scarlet fever, are now under way. Fibrinogen is another of the plasma fractions that Dr. Cohn has isolated. This is the substance which, with the help of Thrombin, a ferment produced when blood is shed, is converted into Fibrin, the clot material. From Fibrinogen, the scientists have made a large variety of plastics which are extremely useful in checking the flow of blood. One of these is fibrin foam, a sponge-like substance that can be placed in open wounds to stop hemorrhages. In the form of an extremely elastic film, Fibrinogen is being widely used in neuro-surgery to repair damages to the brain membrane. Surgeons are taking advantage of the adhesive and

hemorrhage-curbing qualities of this substance in the treatment of burns and in skin grafting. The Isoagglutinins, a fourth fraction, are useful in cases where whole-blood transfusions are necessary. In emergencies, when speed is essential, they may be used to hasten the blood-typing process by interacting with red cells according to their specific blood groups; this technique can save a good deal of time and make some complicated laboratory procedures unnecessary. The functions of the last fraction that Dr. Cohn has isolated, Alpha Globulin, are not completely understood, nor has a definite medical use for the substance been found. Scientists are hopeful, however, that the investigations which have been made possible by the isolation and purification of this component of plasma will lead to the discovery of its physiological function and to some therapeutic values.

In order for the blood to perform its complex and manifold functions, it must remain in a fluid state so that it can circulate freely to all parts of the body. Any interference with this steady flow, even for a comparatively short time, will deprive the cells of the oxygen and nutrients which they need, will cause wastes to accumulate, will prevent the blood from performing its other essential functions, and may cause serious damage to, and ultimate destruction of, the tissues. It is this blocking of circulation by the sludges which appear in disease, injury, and age, that Dr. Knisely and his co-workers have been studying in animals and human beings.

For the most part, the researchers have been using two techniques in making their observations. Thousands of living laboratory animals have been carefully anesthetized and operated upon; and tissues, such as muscle, intestinal lining, brain, liver, etc., have been exposed and examined under the microscope. This has been done in order to learn about the structure, dimensions and natural behavior of the blood and vessels of living internal organs. Since 1941, Dr. Knisely and the other scientists have focused specially-designed microscopes on the delicate blood vessels in the eye membranes of hundreds of living, unanesthetized, unoperated-on men and women. Skillfully used, this procedure causes almost no discomfort to most subjects, and affords the investigators an opportunity to observe the circulating blood under the most normal possible conditions.

In healthy animals, and in fifty medical students and student nurses in prime physical condition who volunteered to take part in the experiments, the blood was found to be flowing freely and speedily through the capillaries. Far from clumping together into sludges, the red cells seemed to repel each other. The inner surfaces of the vessels were smooth and clean, with no white cells sticking to the linings. The walls of the healthy vessels did not leak appreciable amounts of plasma. Despite the narrowness of the capil-

laries, and despite the fact that the junctions between vessels are frequently smaller in diameter than the bodies which must go through them, the red and white cells pass these bottlenecks easily. (They fold over and are temporarily squeezed out of shape.)

III

The picture is vastly different in disease, injury and old age. In every single one of about six hundred unanesthetized human patients diagnosed by practising physicians as having a wide variety of pathologic conditions, Dr. Knisely and his associates have seen the blood cells agglutinated into masses. This changes the blood from its normal fluid state to a circulating sludge. The men and women who were observed during these experiments were suffering from ailments ranging in seriousness from the common cold, chronic sinusitis, and measles, to heart disease, syphilis of the central nervous system, and cancer. All accident cases, even when the injuries were not very severe, showed sludging of the blood. Even in such conditions as hysteria and acute alcoholism, sludged blood was evident. The more severe degrees of agglutination have been exhibited, of course, only in animals during controlled experiments and in persons who were sufficiently ill to have placed themselves under the care of physicians. But no severely ill person has yet been seen who did not have some agglutination; and the investigators stress the point that thus far, they have found completely unsludged blood only in young, healthy animals and men.

There are many ways in which these sludges, interfering as they do with the normal circulation of the blood, can cause injury to the body. Some of the masses are large enough to plug tiny vessels permanently. The damage done by these permanent plugs depends upon their number, their concentration in the blood at any one time, and the particular tissues which they happen to affect. Such masses can, in relatively low concentrations, be utterly devastating over a period of years, months, or even weeks. One young woman who was referred to the experimenters from a psychiatric hospital because she seemed to have some blood disorder in addition to her psychological disturbances had eight small plugs in the arterioles of the membrane of one side of one eye. As she was being examined, more masses came along, temporarily clogged the vessels, and finally moved on. Two weeks later, the researchers examined the patient again and found that three more permanent plugs had been formed. This seemed to indicate that the woman's whole central nervous system was slowly being showered with permanent plugs, each of which destroyed a small volume of irreplaceable nerve cells by cutting off their oxygen supply. This checking of the oxygen supply can cause equally serious damage to other tissues. If the

linings of the blood vessels are affected, plasma begins to leak into the surrounding tissues, causing severe swelling of tissues and grave disturbances in the composition of the blood. This blocking of the vessels, with its consequent leakage of plasma and swelling, is particularly noticeable in patients suffering from rheumatoid arthritis. If the plugs lodge themselves in the tiny vessels which supply the walls of the larger arteries and veins, they may initiate those pathologic changes which are found in men and women with arteriosclerosis and other circulatory diseases.

IV

Another phenomenon which may cause damage to the organism has been observed by Dr. Knisely and his associates. The spleen and the liver contain cells whose function is to remove old and diseased red corpuscles from the blood stream. These bodies never engulf healthy red cells, but they do destroy agglutinated masses. A too rapid and continued ingestion of agglutinated cells by the phagocytes of the spleen and the liver may be a major factor in causing many kinds of human anemias. Moreover, along with the red cells, the sludges contain large amounts of proteins and immunity-bearing Gamma Globulins; and the destruction of these substances may not only cause a severe protein deficiency in the body, but may also weaken the individual's resistance to various infectious diseases.

The investigations of blood sludging may help to explain one of the most serious hazards of illnesses and surgical procedures that involve prolonged bed rest — the formation of thrombi. These are clots, large and small, which frequently form in the veins of bed-ridden patients' legs. If these thrombi become detached, they begin to wander through the circulatory system. When they strike a vital organ such as the lungs, the brain, or the heart, they may cause death. The reasons for the formation of these large blood clots are obscure, but Dr. Knisely and his fellows believe that they may be initiated by the masses of agglutinated blood.

Finally, the leakage of plasma and the destruction of large amounts of blood which are caused by the sludging may give scientists a deeper insight into the problem of shock. Doctors know that decreased blood volume is at least partially responsible for shock. The depletion of the blood stream attendant on sludging may, according to the investigators, furnish a clue toward the understanding of this condition.

Doctors are hopeful that the researches which Dr. Knisely and his group have initiated may lead to the solution of many other medical problems. There are certain nutritional disturbances which have never been satisfactorily explained. There are certain multiple-symptomed diseases related to the blood stream that are still mysteries. There are certain infections which inexplicably become

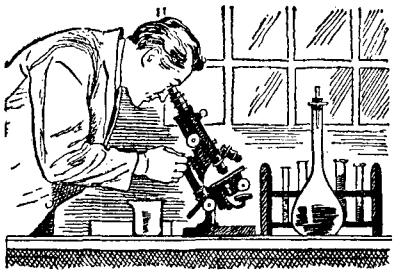
focused in particular organs, such as the kidneys and the heart, which still baffle the medical profession. There are such dreadful scourges as multiple sclerosis which are still highly mysterious in origin. The researches in blood sludging may prove valuable in the understanding of all these diseases. According to Dr. Shepard Shapiro, a prominent New York City blood specialist, "Dr. Knisely's work may prove to be as important to medicine as the discoveries of the bacterial and virus diseases."

One significant possibility that has been opened up by these researches is that they may furnish an explanation for the aging process. When one considers the number of already observed pathologic conditions during which sludges were present, the fact that many sludges could be expected to inflict at least some permanent damage to the body, and the fact that these damages must be cumulative over a long period, it becomes obvious that scientists must now begin to determine carefully how all the damages done to the body by sludges can be related to the aging processes. In connection with this possibility, Dr. Knisely and his co-workers ask certain basic questions: In which different and overlapping combinations can the damages caused by sludges, and the bodily readjustments to these, cause us to age more rapidly? How fast can this damage be done? How do these factors cumulate along with other non-sludge factors in the various aging processes?

To these questions, and to many others that their investigations have raised, Dr. Knisely and his group do not pretend to have final answers. They are still looking for them. What they do maintain is that their observations, experiments, and deductions are evidence that the sludges provide a common, easily understandable explanation for many diseases that damage the bodies of animals and men. Much more research, by many more scientists, will be needed before the mechanism of blood sludging and its relationship to disease is fully clarified. Dr. Knisely and his fellow scientists have put it this way: "One great hope provided by these studies is that, as we learn how to keep blood normally unagglutinated and fluid, vessel walls intact, normal red cells from being destroyed, and adequate blood volume present, many effects of other pathologic mechanisms will stand out clearly, unobscured by the sludge mechanisms. Each will, of course, then receive the undivided attention it merits. The sludges are now ready for study by all the intensive investigative methods our age affords."

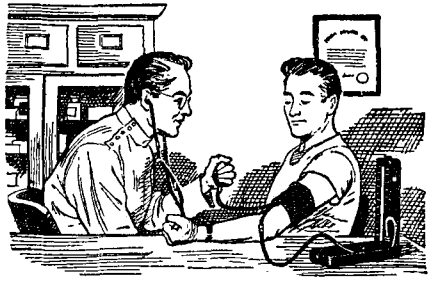
Some Facts About
HIGH BLOOD PRESSURE

BLOOD PRESSURE rises when a person is active. After the strain has passed, the pressure generally returns to its regular level. If it is persistently and excessively above normal, however, that condition is called hypertension—or high blood pressure. This affects the circulatory system and may lead to serious conditions of the heart, brain, and kidneys.



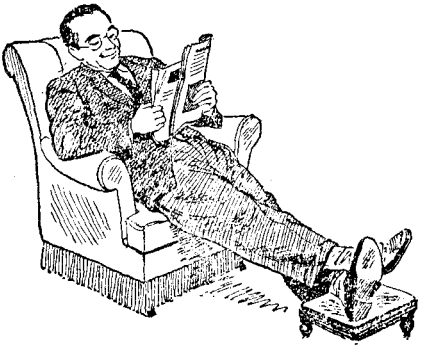
High blood pressure itself is not a disease, but a symptom of some underlying disorder. Medical science is constantly increasing its knowledge of this condition, and is striving for improved methods of treating it. Special diets have sometimes proved effective. In a limited number of cases, surgery has been used. Additional research is concentrating on mental and emotional factors. There is also hope that newly discovered drugs may prove beneficial.

Periodic physical examinations help reveal hypertension early, when doctors say that chances for control are best. Such check-ups may also discover possible infections which may be causing the condition.



As a result of physical examinations,

the doctor may make suggestions for improving your health, such as eating wisely and *keeping weight down*. The latter is especially important, for high blood pressure is more than twice as common among fat people than it is among persons of normal weight.



In many high blood pressure cases, the best "medicine" is often simply *moderation in every physical and mental activity*. The patient may be advised to work and play at a slower pace, to avoid emotional strain, and to get plenty of rest and sleep. This helps to lessen the demands on the circulatory system, and may lower blood pressure.

Today, under good medical guidance, the outlook for people with high blood pressure is better than ever before. By carefully following the doctor's advice, they can often avoid complications and look forward to long, useful lives.

• • •

Aiding in the development of more effective measures to help combat high blood pressure is the Life Insurance Medical Research Fund, supported by 148 Life Insurance Companies. This fund is making grants for research in diseases of the heart and blood vessels, including high blood pressure.

For more information, send for Metropolitan's free booklet, 59-L, entitled, "Your Heart." This contains many facts about high blood pressure and diseases related to the heart.

Metropolitan Life Insurance Company

(A MUTUAL COMPANY)

1 MADISON AVENUE, NEW YORK 10, N. Y.

TO VETERANS—IF YOU HAVE NATIONAL SERVICE LIFE INSURANCE—KEEP IT!

ROBERT E. LEE: THE SOUTHERN SAINT

BY RICHARD O'CONNOR

THE year 1948 saw the South rally again around Confederate flags, recall the hallowed names of 1861–65, and raise the cry of States Rights as opposed to Civil Rights. The name of Robert E. Lee was invoked, of course, as the most compelling of all Confederate touchstones.

The shade of Lee, looking down on this faintly reminiscent scene, with the slogans though not the fervor of the first Secession, was probably less than enthusiastic. By his own words, the cause of Secession never much enlisted his sympathies, whether the cause was concerned with States Rights or the defense of slavery as an institution. He had never questioned his loyalty to the Union until the war crisis was actually at hand in 1861. Only then, when his native state of Virginia had seceded and was obviously about to be invaded, did his devotion to the Federal government evaporate.

"Virginia to him was the world" — the world of Arlington, the world of Washington, the tranquil world of his beloved family . . . and for it he foreswore command of the Union armies and every material advantage that went with it. He and Virginia were inseparable. This "love of place" is an American characteristic; it has been said that through all our wars American soldiers have fought for a stretch of red clay in Georgia, or for a New England valley, as much as for the United States as a whole. It was this parochial element that was Lee's greatest weakness as a citizen, and his greatest strength as a Confederate soldier.

His service to the Confederacy, therefore, was limited, as can be seen from his statement on resigning from the Federal army — "Save in defense of my native state, I never desire to draw my sword." True, he led invasions of Maryland and Pennsylvania, but these can fairly be said to have been only aggressive defense of Virginia. He refused to go West at a critical period to take over the Confederacy's forces there, though the weaknesses in the Western command resulted in collapse and foreshadowed Lee's own surrender in the East. The

RICHARD O'CONNOR *is the author of* Thomas: Rock of Chickamauga, *published recently by Prentice-Hall; of* Hood: The Self-Made Cavalier; *and of many magazine articles, including a reappraisal of General Sherman which appeared in the* MERCURY *last November.*