Extracted from the American Journal of the Medical Sciences,
September, 1925, No. 3, vol. clxx, p. 420

INCREASED PERMEABILITY OF VESSEL WALLS AS A FREQUENT CAUSE OF PULMONARY HEMORRHAGE.*

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Blood spitting is a frequent symptom of pulmonary disease, particularly pulmonary tuberculosis. A very large majority of all patients suffering from active pulmonary tuberculosis expectorate blood sometime during their illness.

It was formerly generally accepted that blood in the sputum meant a destruction of a portion of the wall of a pulmonary vessel, the variation in size of hemorrhages depending upon the size of the vessel in which the opening occurred.

More careful observation of tuberculous patients, however, shows that blood coming from the lungs does not always indicate the same underlying condition. Ulceration of the walls of vessels of some considerable size and rupture of aneurysmal dilatations in cavities occur now and then and cause severe or even fatal hemorrhages. Injury to the walls of tiny capillaries is also a frequent cause of bleeding; but the great majority of pulmonary hemorrhages which occur, evidently from their very nature, are not due to either of these causes. They usually occur and recur under certain conditions, the most common of which are changes in weather, the presence of acute respiratory infections and during the menstrual cycle. They are usually small in amount, consisting of only one or two mouthfuls, but sometimes they are more copious. They frequently persist over several days and are apt to recur when the same or similar conditions again arise. Many of them occur in the early morning hours.

A tendency for tuberculous patients to spit blood during the menstrual period has long been recognized. It has been spoken of as a vicarious menstruation. This, we now know, to be an incorrect explanation. This blood spitting is a part of the general increase in severity of symptoms which occurs at this time, and is undoubtedly due to increased pathologic activity in the tuberculous foci. In explaining this according to the theory of Jobling and Peterson,[1] we assume that prior to the time that the menstrual disturbance occurs the enzymes which are instrumental in breaking down the tuberculous tissue are bound by antienzymes. These latter are not specific. When the enzymes which accompany the menstrual cycle enter the blood stream then a portion of the antienzymes which are binding the former leave them and bind those which accompany menstruation. The former, released, cause

* Read by title at the Forty-second Annual Meeting of the American Climatological and Clinical Association, Washington, D. C., May 5 and 6, 1925.

increased activity in the tuberculous areas. This increased activity at times appears as increased permeability of the capillaries and results in the escape of blood.

Observations made by different observers, the staff of the Phipps Institute,[2] and more recently Walsh[3, 4] and Montgomery[5] have called attention to an apparent relationship between certain hemorrhages and the presence of pneumococci and other organisms causing acute respiratory infection. This is too well established now to be questioned. I have noted it frequently. I have seen two quite severe hemorrhages accompanying tonsillitis, and many accompany the common acute respiratory infections. The writer[6] previously stated in describing this type of hemorrhage: "I look upon this type as being due to a congestion much the same as we see in pneumonia and heart lesions. Is it not possible, however, that it might be due to toxic action?" And later:[7] "The theory of toxic action seems to me to be the one which offers the best explanation. Such types of hemorrhage rarely occur except where the disease is active. It is not at all improbable that the hemorrhage is part of a collateral inflammatory exudation."

Browning[8] made a study of symptoms including hemorrhage in its relationship to changes in weather at the Pottenger Sanatorium, and he concluded that there was a definite relationship between their occurrence and barometric changes. Hemorrhages of all kinds are affected by weather conditions. Sudden marked changes from wet to dry, or from dry to wet, fog, sudden hot or cold spells are accompanied by an increase in incidence of blood spitting, which can be readily observed in institutions where a tuberculous population of 100 or more exists.

Recent advances in biophysics and studies on the physiology of the circulatory system suggests a rational explanation for some of the types of bleeding here discussed. Krogh[9] has discussed the effect of capillary poisons which cause such a dilatation of the vessel walls as to permit of ready passage of the constituents of the blood into the tissues. Among substances classed as capillary poisons he mentions certain salts of gold and arsenic, histamin and sepsin. Doubtless there are many substances having such action. Clinical evidence shows that many acute respiratory infections are accompanied by blood spitting. The type of acute respiratory infections which have been common since the pandemic of influenza in 1918 have not only been the cause of blood spitting in many frankly tuberculous patients, but in some in whom I could find no evidence of active tuberculous disease. Either the poisons from the tubercle bacilli or the tuberculous process or that from the germs causing the acute infection could probably act as direct capillary poisons, or there could be an increased permeability of the vessel walls as a result of the increased activity of the local cells. The increased local activity in this type may also be accounted for by the same enzyme-antienzyme action as mentioned in connection with menstruation.

Increased activity is accompanied by an increased permeability of tissues (Lilly[10, 11] and Mathews[12]), so it is quite easy to understand how infections and menstruation, by causing selective action upon the already diseased areas, may have a tendency to cause increased activity in the areas of infection. Cells which are injured are more sensitive than normal cells, consequently an amount of stimulation which is not sufficient to affect normal cells might easily produce effects in cells which previously have been sensitized by disease so as to cause such a degree of increased permeability as to allow the escape of blood or sanguineous fluid.

It is more difficult to explain the manner in which the blood spitting which accompanies changes in weather is produced. This inability to explain on our part is doubtless partly due to our ignorance of the effects upon the body caused by changes in weather and partly to a failure to appreciate the degree of physiologic adaptation which is required on the part of the body to preserve equilibrium during such changes, and especially to a failure to appreciate the handicap to adaptation which is experienced by those cells which are the seat of disease.

Think of the change that must be effected to cool the air from 120°, 200° and 300°, as is found in heated ovens, to 98.6°, the normal temperature of the body; or to warm it from zero or a −20° or 40° to that of the normal 98.6° of the body; or of saturating an air with moisture when its relative humidity is reduced to a minimum; or of the adjustment of the body that is necessary for it to function normally in both bright sunshine and in the presence of cloud. Think of the difference in stimulation that attends these various conditions, and the effects produced upon the vessels of the respiratory passages as a result of them.

The influence of the varying content in light rays and in electric units under conditions of storm and pleasant weather, and the changes in barometric pressure under the same conditions, are immense factors in disturbing physiologic action. The normal 14.7 pounds of pressure per square inch of body surface which is found at sea level changes enormously at these times. Huntington[13] says the increase of 1 inch in barometric pressure is equivalent to adding a weight of 1,000,000 tons to each square mile of the earth's crust. This same relative change in pressure is experienced by the human body and means an additional ton of pressure. A decrease in barometric pressure removes weight in the same proportion. These changes call for enormous adjustment. Think what they mean to the superficial body structures and to mucous membranes.

Increased permeability shows itself most frequently in the bronchial mucous membranes, but it is also frequently noticed in the nasal mucous membrane when no apparent inflammatory condition is present.

The type of hemorrhages which depends on these weather changes is most apt to occur at the time of day when atmospheric pressure

is low. There are two maximum and two minimum periods of atmospheric pressure each day, and it is interesting to note that the lowest pressure is found in the early morning (about 4 A.M.) hours, and that this is the time when most hemorrhages of this type occur. The second minimum occurs in the afternoon (about 4 P.M.), and this is another time in the day when hemorrhages occur.

According to biophysics, activity in body cells is an electric phenomenon brought about by a difference in potential between the two sides of the cell membrane. The point of injury or the point of stimulation of the cell assumes a negative charge, thus affording the condition necessary for starting an electric reaction. Increased electric reaction, increased cellular activity and increased tissue permeability are concomitant states which accompany action and reaction of tissues.

Summary. Acute infections of the lung are apt to produce their greatest effect at the point where the tissues are now or have been injured by tuberculous disease. This causes increased activity and permeability of tissues, including bloodvessels, which at times result in conditions which permit the passage of blood through the vessel walls.

The menstrual enzyme in some manner causes increased activity in local tuberculous processes, which is accompanied by increased permeability.

Certain weather changes, the exact factors in which we do not know, affect all tissues of the body, but particularly those of the lung which have been injured as a result of active disease, and cause the blood to pass through the capillaries. This is particularly true of those injured by tuberculous infection.

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