III.

HEMOPHILIAC TYPE HEMORRHAGE—TREATMENT BY TRANSFUSION.

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This paper is presented to emphasize the usefulness of transfusion in the control of hemorrhage in patients whose clotting time is abnormally slow, and in whom the bleeding persists as a capillary oozing after all mechanical means for hemostasis have failed. Its scope is limited entirely to the treatment of hemophiliacs, or perhaps more properly to patients whose blood clotting period is abnormally long.

In reality, hemophilia is a very rare condition, with an extremely interesting and extensive literature. The first description of the disease can be found in the Crerar Library in the original article by John G. Otto, early in 1803.¹ The "Natural History of the Village of Kinderbrook" immediately follows, showing the versatility of this publication. Otto, according to his bibliography, read by Isaac Parrish, M. D., the physician in his last illness, before the College of Physicians of Philadelphia by appointment March 4, 1845, was one of the earliest physicians of Philadelphia "to confine himself wholly to the practice of medicine, avoiding surgery and obstetrics." His observations on "An Hemorrhagic Disposition Existing in Certain Families" are stated in precise, well chosen English. With but few additions it would be a classic description even today.

"About seventy or eighty years ago, a woman by the name of Smith settled in the vicinity of Plymouth, New England, and transmitted the following idiosyncrasy to her descendants. If the least scratch is made on the skin of some of

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them, as mortal a hemorrhage will eventually ensue as if the largest wound is inflicted." He speaks of the blood being in a "high state of effervescence," of the various remedies that have been tried in vain, among them being "the bark, astringents used topically and internally, strong styptics and opiates. A few years since the sulphate of soda was accidentally found to be completely curative of the hemorrhages I have described. An ordinary purging dose, administered two or three days in succession, generally stops them: and by a more frequent repetition is certain of producing this effect. The cases in which the most powerful, and apparently the most appropriate remedies have been used in vain, and those in which this mode of treatment has been attended with success, are so numerous that no doubt can exist of the efficacy of this prescription. Deceptions may take place from accidental coincidence: but when a complaint has often occurred, and been almost uniformly fatal, without the administration of a certain remedy, and has constantly yielded when it has been given, skepticism should be silent with regard to its utility. Nor should our inability to account for the fact upon the theory and principles we have adopted be conceived as a sufficient reason for disbelieving it."

The proceeds: "The prescription being in the Smith family and the cases that have been attended by physicians not being very numerous, it is impossible to ascertain the various states of the system in which it has been given, or to form any correct conclusions regarding its manner of acting. No experiments have been made on the blood to discover if any, or what changes take place in it."

"It is a surprising circumstance that males only are subject to this strange affection, and that all of them are not liable to it"—although females are exempt, they are still capable of transmitting it to their male children, as is evidenced by its introduction, and other instances, an account of which I have received from the Hon. Judge Livemore, who was polite enough to communicate to me many particulars upon this subject. This fact is confirmed by Drs. Rogers and Parker, gentlemen of character, residing in the neighborhood. When cases shall become more numerous, it may perhaps be found that the female sex is not entirely exempt."

Benjamin Rush, Dr. Otto states, had seen two cases in his own practice and recites the history of a Maryland family of six children, four of whom died of bleeding from trifling scratches or bruises. A small pebble fell on the nail of the forefinger of the last of them when at play, being a year or two old; in a short time the blood issue from the end of that finger until he bled to death.

While Otto's paper was the origin of our knowledge of this subject, hemophilia was evidently known to the ancients. Abacusic or Asaharavius, the greatest surgical writer of the Moorish period, stated that in a certain village there were men, who when wounded only slightly, bled to death. Alexander Benedictus, 1539, tells of a Venetian barber who bled to death from a trivial wound on the nose inflicted by his own scissors.

Most of the literature has come from America. The most notable exceptions are the extensive monographs of Ludwig Grandidier,⁴ Wickham Legg⁵ and Bulloch and Fields.

The latter two define hemophilia as a "disease characterized by excessive or chronic liability to immoderate hemorrhage. The liability is hereditary and, in our opinion, based upon the published evidence, is confined to the male (bleeder) but transmitted by the female (the conductor)." This is generally known now as Nasse's law.⁶ The characteristic hemorrhage is a trickling, oozing from a surface and not from any one large vessel proceeding from a traumatism that would be of any consequence to a normal individual. It is always traumatic.

The most frequent sites are the nose, mouth (after extraction of teeth), joints, umbilicus in the newborn and penis following circumcision.

Cause and Occurrence.—The essential cause of hemophilia seems to lie with the blood platelets. The walls of these cells apparently are not sufficiently soluble to liberate their intracellular protoplasm (thrombokinas?) which is necessary for blood coagulation.⁷ Either the thyroid or liver or both may be responsible, for these alone, of all the body tissues of the hemophiliac, fail to promote blood coagulation.⁸

Frequently troublesome hemorrhages are accredited to the hemophiliac diathesis, and many patients are designated as

bleeders, in whom the clotting is well within the normal limits. In these cases adequate surgical means of hemostasis have not been used. They might well be designated as surgical hemophilia.

True hemophilia in reality is a very rare condition. Grandidier⁸ states that there were only ninety-three families of bleeders in the entire German empire in 1877, with but two two hundred and fifty-eight members affected. With the more accurate present laboratory methods this number would undoubtedly be decreased very materially were these cases examined at this time, especially since twenty-two of his cases were females.

Tendency to hemorrhage is seen in many of the following diseases. Of these jaundice is the most common; others of less frequent occurrence are typhoid fever, anemias, leukemias, purpuras, Barlow's disease, peliosis rheumatica and essential hematuria.⁹ Severe bleeding may follow diphtheria, quinzy, yellow fever, influenza, and surgical procedures, especially in the throat and nose (secondary hemorrhage). These cases must not be confused with true hemophilia.

Case Report.—Fred A. B——, a married man, thirty-nine years of age, came to the writer in July, 1918, complaining of recurrent head colds and slight attacks of sore throat followed by rheumatic pains. His tonsils were enlarged. From their crypts pus could be freely expressed. His nasal septum was sharply deflected to the left low down. Family and personal histories were given as generally negative with the exception of a severe attack of smallpox he had suffered years ago. Syphilis was denied. His general physical examination was negative. His nose and throat work was done under general anesthesia a few days later. The submucous resection (after Killian) was confined almost entirely to the cartilages. One Bernays sponge was inserted into each nostril. The flaps were not perforated. The tonsils were removed by dissection and snare. The bleeding was less than usual from each. Both tonsil fossæ were dry when the patient left the operating room. The operation was commenced at 8 a. m. and finished at 8:30 a. m.

Five hours later (1:30 p. m.) the nurse reported that the patient's bleeding, which had commenced about half an hour

after his return to bed, was not stopped. At 2:30 p. m. another Bernays sponge was placed on each side of the nose. At 5:30 the bleeding from the nose was continuing at about the same rate—i. e., twenty-five drops a minute, with some trickling back into the throat. The sponges were removed, the flaps separated and the septal cavity was carefully suctioned and sponged in an effort to locate the bleeding point. This was unsuccessful. In about half a minute the cavity would slowly fill up with blood which appeared to well up from all over. The Bernays sponges were reintroduced with strips of tannic acid gauze packed tightly against their outer sides.

At 8:30 p. m. the bleeding was still continuing at the same rate from the nose and mouth. The posterior nares was now seemingly packed on the left (operated) side and the sponges and tannic acid gauze were replaced. Coagulation period by the glass pipette method was taken and found to be fifty minutes. Hemoglobin was eighty per cent. The patient was feeling well, remarkably well in spite of his very considerable loss of blood.

At 9:30 p. m., twenty cc. of normal horse serum was given deep in the muscles of the abdominal wall. At 11 p. m. (fifteen hours after the operation) the blood was still dripping from the nose, about twenty-five drops a minute, with a considerable amount running back into the throat. Dr. Henry W. Ablemann transfused one hundred cc. of blood from the arm of the patient's sister, who was mistaken for his sister-in-law. The bleeding seemed to be less, and the patient was returned to his bed after having received one-quarter grain morphin.

At 8 a. m. (twenty-four hours after the operation) blood was trickling from his nose and running back into his throat at the same rate. A second transfusion was made—this time from his sister-in-law instead of his sister. Five minutes later the bleeding had stopped completely. The coagulation period was now five minutes. The hemoglobin was seventy per cent. The patient was feeling splendidly and asking for something to eat.

On questioning the patient's father closely some vague history of severe bleeding was elicited in an uncle on his

maternal side. The patient's sister, in the first and unsuccessful donor, is a young unmarried woman. It will be extremely interesting to note whether or not she proves to be a conductor of hemophilia. Her coagulation period was six minutes. She had had an uneventful abdominal section within the year. The second donor's (sister-in-law) blood clotted in eight minutes.

The author is fully aware of the fact that the above case does not entirely meet the requirement laid down by Bullock and Fildes.⁵ These excellent investigators maintain that no single hemorrhage, however severe or inexplicable, can properly constitute a diagnosis of true hemophilia—only repeated bleedings either from birth or early childhood are sufficient for this.

In conclusion, however, some interesting speculations arise:

1. Can the coagulation period of non-hemophiliac blood be so long as to cause a hemorrhage such as this patient had? Is the hemophiliac himself always a hemophiliac or will his blood at times clot normally or nearly so?

2. Are the tissue juices that favor coagulation more abundant in the throat than in the nose? This would explain the dry tonsil fossae.

3. How lasting may the results of transfusion be? Two months later this patient had an uneventful tooth extraction.

4. Enormous quantities of blood can be lost, if the bleeding is slow. In this case probably more than four quarts of blood was lost in twenty-four hours by nose and mouth. At the end the hemoglobin was 70 per cent. and the red cells three and one-half million.

5. Transfusion in such cases, seems to be the logical and sure way of stopping the bleeding. Abelmann's splendid technique¹¹ reduces what was formerly a formidable major operation to a very simple, bedside if necessary, procedure.

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