SOME FORMS OF HÆMORRHAGE WHICH ARE DIFFICULT OF EXPLANATION.¹

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AS I have been much interested in certain forms of hæmorrhage, I have taken this subject for consideration. Usually the explanation of the bleeding is easy—for example, an aneurysm ruptures, or tubercular ulceration eats into a vessel and the patient has hæmoptysis, or under the stress of a heightened blood pressure a diseased cerebral vessel gives way. It is not difficult to suggest why bleeding should follow an infarct, nor why when the vessels generally are greatly over-full it should occur in polycythæmia, nor why when they are locally over-full, as those of the portal area may be in cirrhosis, the patient should have hæmatemesis. It is easy to understand why, as the coagulation of the blood is greatly retarded in those who suffer from hæmophilia, minute injuries to vessel walls should lead to serious hæmorrhage.

When an occurrence is common we become so familiar with it that we are inclined to forget that we do not understand it. Rarely do we stop to reflect how extraordinary it is that if one ciliary muscle is paralysed as a result of diphtheria so is the other; if one anterior tibial nerve is inflamed by alcohol so will the other be. In the same way many varieties of hæmorrhage with which we are quite familiar may well cause much thought.

Let us first direct our attention to purpura. Here the bleeding is under our very eyes, and one thing is quite certain—namely, that the red cells cannot come through the walls of the vessels unless there is a solution of the continuity of those walls. No amount of talk about coagulation can explain hæmorrhage; deficient coagulation may explain why bleeding does not stop but not why it began; for it to begin there must be damage to the vessel walls sufficiently great to let blood corpuscles through. Purpura may occur as a result of giving a patient drugs—notably iodide of potassium, chlorate of potassium, and copaiba—by the mouth. It is difficult to resist the belief that these poisons, or derivatives from them, circulating in the blood lead to damage of the walls of the cutaneous vessels and consequent purpura. In the same way poisons or toxins circulating in the blood and causing local damage to minute vessels probably explain why septicæmia and some of the exanthemata are occasionally purpuric, although here it may possibly be that the micro-organisms themselves cause the bleeding either directly or by the formation of infarcts. Purpura is met with in scurvy, cirrhosis of the liver even if there is no jaundice, severe jaundice, and after the administration of serum, and in each instance it is extremely likely that there is some poison circulating in the blood which damages the minute vessels of the skin. Acute rheumatism, a common cause of purpura, is certainly a specific fever, and therefore the purpura may be toxic, as it may be in the exanthemata. Inasmuch as there must be a solution of vessel walls for the production of purpura, and several drugs cause purpura, we may assume that these drugs or their derivatives circulating in the blood act on the minute vessels so as to cause a solution of continuity and consequently hæmorrhage, and as no better explanation is forthcoming for purpuras—e.g., purpura hæmorrhagica and Henoch's purpura, in which there is no direct evidence of a toxin which damages vessels—we may, as here also there must be a solution of continuity of minute vessels, assume, without violent improbability, that in these varieties of purpura there are circulating in the blood toxins which can damage vessels in this way. It has been stated that the seat of the hæmorrhage in purpura is in the minute veins just at the point where they leave the subcutaneous tissue and enter the skin proper; they are especially weak at this point, hence when damaged they give way there.

In all purpura there must be a damage to vessels, and very often this damage extends to the vessels of other regions than the skin. Thus we have hæmorrhages into the gums and muscles in scurvy, gastro-intestinal hæmorrhages in Henoch's purpura, and epistaxis with internal hæmorrhage in many places in purpura hæmorrhagica, and internal hæmorrhages in jaundice. We have indication that

some poisons damage some vessels more easily than others—for example, purpura is rare in scurvy, but hæmorrhages into the gums and muscles are common. In most cases of purpura hæmorrhagica bleeding takes place only into the skin; and in cantharides and turpentine poisoning, although the poisons must circulate in the blood to reach the kidneys, yet the damage to the vessels is usually confined to those of the kidney with consequent hæmaturia. When a poison circulating in the blood commonly selects some particular structure on which to act, we must assume that the chemical or physical nature of that structure is different from that of otherwise similar structures in such a way that the poison can produce results on it and not on them. For example, there must be some chemical or physical difference between the anterior tibial and musculo-spiral nerves, or else it could not be that if alcohol is going to cause neuritis it invariably picks out the anterior tibial most easily; on the other hand, if lead is going to cause a neuritis it almost invariably picks out the musculo-spiral before other nerves. In the same way there appear to be differences in the walls of the vessels in different parts, for some poisons circulating in the blood stream damage some vessels, and others damage others.

Having called attention to the fact that hæmorrhages under the skin may occur quite apart from any gross cause, that hæmorrhages inside the body may be associated with hæmorrhages into the skin, and that certain poisons act on particular vessels so as to cause them to rupture, let me now direct your thoughts to some mysterious internal hæmorrhages: by far the most remarkable is menstruation. The fundamental fact is that at stated periods the walls of the vessels of the uterine mucous membrane undergo some change which enables the blood to burst through. What this change is we do not know; some have spoken of it as a degeneration, but considering that the phenomena of menstruation and heat are normal it is doubtful whether degeneration is the right word; but at any rate in a few days the vessel wall undergoes an alteration which leads to a weakening, the blood ruptures into lacunæ in the uterine mucous membrane, and tearing through the epithelium passes into the uterine cavity. We know that the menstrual flow is controlled by a hormone secreted by the ovary, for excision of both ovaries is followed by a cessation of heat or menstruation, and there is considerable evidence that the transplantation of an ovary from another subject into one who has ceased to menstruate as a consequence of the loss of both ovaries will restore heat or menstruation. This function of the ovary is not derived from the corpus luteum, but it is not decided whether it is dependent upon the follicular epithelial cells or the interstitial cells. Formerly it was commonly believed that menstrual flow could take place from other organs than the uterus, and the belief has hardly died out. As recently as 1897 Oser stated that this might occur, and, indeed, it is admitted in a very recent text-book, but I think you will agree with me there is no real evidence in favour of vicarious menstruation, and therefore we must conclude that the substance secreted by the ovary which is carried by the blood to the uterus, where it causes such a change that the blood in the uterine vessels can rupture them, acts on the uterine vessels only, a fact which strongly suggests that the uterine vessels are different from other vessels, and which harmonises with the opinion expressed a few minutes ago that the most satisfactory explanation of some forms of pathological bleeding is to believe that it is caused by the circulation in the blood of toxins which act in particular on the walls of the vessels through which the blood ruptures.

I should now like to direct attention to some facts which support the belief that pathological hæmorrhage due to some substance circulating in the vessels and damaging the walls of the minute vessels may occur inside the body only. Everyone with even a moderate experience of work in the post-mortem room must be familiar with subpleural ecchymoses and those which occur in the alimentary tracts especially the stomach. Among 2246 post-mortem examinations I find them noted in 172, and of these 68 were performed upon those dead of an acute infective disease, such as pneumonia or pyæmia. In some instances these ecchymoses might be caused by obvious emboli, backward pressure, high blood pressure, or arterio-sclerosis, but a very large number remain in which no such explanation holds, and it is quite possible that some toxin damages minute vessels, but it may be that micro-organisms acting locally

¹ Abstract of an address given at the annual meeting of the past and present students of the University of Durham College of Medicine, held at Newcastle-on-Tyne on Feb. 6th, 1912.

are the cause. Let us next consider the condition to which the term *gastrostaxis* has been applied. Many authors have been struck with the frequency with which young women vomit blood—for example, Dr. E. W. Goodall found that out of 36 cases of hæmatemesis under 30 years old 27 were women and 9 were men. Formerly, this was ascribed to vicarious menstruation; when this explanation was discarded these bleedings were considered to be due to gastric ulcer, and accordingly we were taught that gastric ulcer was far commoner in women than in men, and it was especially seen in young women. But suspicion as to the correctness of this view was aroused by the facts that in men gastric ulcer was commoner at a considerably older age, and gastric ulcers found in the post-mortem room were no commoner in women than in men. Then several cases were operated on for hæmatemesis and no ulcer was found, and cases were published in which a careful search after death had failed to demonstrate the presence of any ulcer. When such a case was examined during life the blood was seen by several surgeons to be oozing from many minute points usually grouped together.

That there is a disease far commoner in young women than in older women or men characterised by dyspepsia, pain, vomiting, and hæmatemesis is allowed by most recent authors who have written on the subject. I have published many such cases.² Since I did so others have come to my notice. Dr. A. E. Boycott has given me particulars of a woman, aged 35, who had indigestion with severe hæmatemesis in 1905, and in 1906 when it was nearly fatal the stomach was opened, and all that was seen wrong was a large area of congested bleeding mucous membrane. Mr. J. S. Watson tells me of a woman, aged 25, who for many months suffered from pain in the stomach, nausea, vomiting, and hæmatemesis. She was thought to have a gastric ulcer, but on opening the stomach at an operation no trace of an ulcer or cicatrix could be found. Hæmatemesis and melæna have continued since the operation. A woman, aged 44, had been in Guy's Hospital on many occasions for pain, nausea, vomiting, and hæmatemesis; she died outside. The late Mr. W. F. Hearnden sent me the stomach. I could find no trace of any ulcer or cicatrix. A man, aged 36, seen with Mr. A. H. Card. Hæmatemesis and melæna were so severe that we thought he had a duodenal ulcer. At an operation Mr. Arbuthnot Lane examined the stomach and duodenum most carefully, but no sign of an ulcer could be seen. This condition has been called *gastrostaxis* and the explanation of it that has always appealed to me has been that the disease consisted in a giving way of the walls of minute vessels, that blood first effused under the gastric epithelium broke through this and hence the bleeding. If this view is correct we must suppose the weakening of the blood-vessels to be due to an endothelial toxin and then these cases are allied to the conditions previously mentioned in this paper, in some of which, e.g., *purpura hæmorrhagica*, hæmatemesis is by no means uncommon; we should then have *purpura hæmorrhagica* a disease in which an endothelial toxin acted on the vessels in several situations, and *gastrostaxis* a disease in which an endothelial toxin acted only on the vessels of the stomach and occasionally on those of the intestine, for sometimes the bleeding occurs also in the intestine. Thus Dr. A. G. Gullan³ reports the case of a girl who had all the symptoms of gastric ulcer, including hæmorrhage; she died suddenly. The stomach showed numerous small hæmorrhagic erosions scattered over its surface, which was congested in certain places; similar erosions were found in the duodenum and jejunum and there were subperitoneal hæmorrhages. Dr. W. P. Herringham also records cases in which the bleeding occurred from the duodenum as well as the stomach, and I have recorded some.⁴ As the blood bursts through the gastric epithelium there must be minute erosions, and Dr. C. Bolton, while he agrees that there is a condition most often seen in young women and characterised by dyspepsia, pain, vomiting, and hæmatemesis, inclines to the belief that some or all instances of *gastrostaxis* are really instances of minute gastric ulcers. The matter is not easy to decide, for the difference between minute ulcers and minute erosions is difficult to make out without the most careful microscopical examination; and the opportunities of this are few, for surgeons have rightly largely given up opening the stomach for gastric hæmorrhage, and the condition we are describing is rarely fatal;

but at any rate it must be admitted that an endothelial toxin is quite a likely explanation for these cases, and it would perhaps best explain the cases in which the oozing of blood occurred in other parts of the alimentary tract than the stomach. Further, the possibility that a toxin causes the hæmatemesis is supported by Dr. J. J. Pringle's⁵ and other cases of urticaria accompanied by hæmatemesis, for urticaria is often toxic.

Many a time it has happened that a physician or surgeon has, on account of hæmaturia, thought that a stone or new growth existed in the kidney, but a most careful exploration, or in some cases excision, of the kidney has failed to find any satisfactory explanation for the hæmaturia. These are examples of what has been called renal epistaxis, or, to use a phrase more widely employed, essential renal hæmaturia. There are so many causes for hæmaturia that scepticism as to the existence of essential renal hæmaturia is justifiable, but there is no doubt that it exists. I have recently collected several cases.⁶ Senator says: "There still remains a group of cases in which nothing can be found in the kidneys to account for the hæmorrhage." Herrick gives the case of a man aged 45, who had had hæmaturia for ten months. The cystoscope showed that the blood came from the right kidney; nephrotomy revealed nothing abnormal. The kidney was healthy histologically. Klemperer describes the case of a young man aged 22, who had hæmaturia which proceeded as shown by the cystoscope from the left kidney. Nephrectomy was done and the kidney was perfectly healthy both to the naked eye and microscopically. Wulff and Schenk describe similar cases, the bleeding coming from only one kidney, which both to the naked eye and histologically was normal. I could quote other cases from medical literature; they will be found in the article on essential hæmaturia to which I have referred. I have carefully read the whole of the literature to which I have access in London, and I think there is no doubt that bleeding may take place from the kidney without there being any evidence to the naked eye or microscope that the organ is diseased. For example, a woman, aged 35, was admitted under Mr. C. J. Symonds for profuse hæmaturia; it appeared that the blood came from the right kidney. This was excised; it was healthy both to the naked eye and histologically. I wrote to the patient 27 months after the operation, and she said that her health and weight had improved greatly; she had had during this time one attack of hæmaturia presumably from the other kidney. This condition occurs both in women and men, but more often in men. The patients are usually under 30; it is very rarely fatal. I submit that the most feasible explanation of these cases is that in them a poison—analagous to the menstrual hormone—is formed somewhere at intervals, and this reaching the kidney by the blood, and having a special affinity for the minute renal vessels so damages them that they rupture and the blood escapes; if this is so these cases have the same explanation as those of bleeding from other parts of the body which we have been considering.

It is well known that hæmatemesis is an early symptom of splenic anæmia and that it occurs long before the final stage of hepatic cirrhosis. May it not be that here we have absorbed from the spleen and carried to the stomach by the blood, a toxin having the property of damaging the gastric vessels and so letting blood through and causing hæmatemesis?

I have left till last the mention of epistaxis, for I have very little experience of it unless as a complication of well-known disease, but there is a very widespread belief that it is especially common in boys at the age of puberty who are perfectly healthy. If this is so, it seems difficult to resist the explanation that the epistaxis is due to the circulation in the blood of an unknown substance which has the special property of damaging the vessels of the nasal septum so as to cause hæmorrhage from them.

I hope you will not consider this address too fanciful, but with the strong evidence we have that the menstrual flow is provoked by a hormone secreted by the ovary, it seems to me worth while to consider whether any pathological hæmorrhages might not be produced in a similar way, and I think it possible that they may, being caused by endothelial toxins which act on the walls of the vessels from which the bleeding comes.

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² *Gastrostaxis*, THE LANCET, Nov. 3rd, 1906, p. 1189.

³ The General Practitioner, Dec. 8th, 1906.

⁴ St. Bartholomew's Hospital Reports, vol. xlv.

⁵ Transactions of the Clinical Society of London, vol. xviii., p. 143.

⁶ Essential Renal Hæmaturia, Quarterly Journal of Medicine, vol. iv. No. 16.