An Address

ON THE

CLINICAL SIGNIFICANCE OF SPONTANEOUS HAEMORRHAGE AS AN EARLY SIGN OF DISEASE.

DELIVERED TO THE NEWCASTLE-ON-TYNE CLINICAL SOCIETY.

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ON this occasion I wish to draw attention to the significance of haemorrhage as an early sign of disease. I shall also give some illustrations which show that unexpected haemorrhage, even when copious in amount, may sometimes be followed by no untoward results.

It may be considered that the importance of haemorrhage is already sufficiently recognized, not only by medical men but by people in general, as the occurrence of haemorrhage without any obvious cause, such as an injury, is naturally an alarming event, which usually leads to medical advice being sought at the earliest opportunity. Unfortunately, we meet with cases in which the importance of, at any rate, small haemorrhages has been underestimated, and so the onset of serious disease has escaped detection until irreparable damage has been done. Thus, how often has the neglect of the warning given by slight or irregular haemorrhages from the rectum or from the uterus in cases of carcinoma resulted in the disease reaching such an advanced stage before a medical man is consulted that removal is no longer possible? I shall not speak of losses of blood due to some easily recognized cause, such as an injury, or a definite disease such as pulmonary tuberculosis, the existence of which has already been recognized. The haemorrhage I propose to consider is that which occurs unexpectedly, either when the patient is apparently in good health or in association with symptoms which do not account for its onset.

Haemorrhage from any source may be of importance for two separate reasons. Firstly, it may be an important indication of disease owing to the site at which it occurs and the circumstances in which it arises, quite apart from the amount of blood which is actually lost. Secondly, it may be of importance owing to the quantity of blood which is lost and the secondary anaemia which this loss entails. Under many conditions the importance of a haemorrhage is proportional to the amount of blood which is lost, but this is by no means always the case. A small haemorrhage may prove to be of far greater importance than a large one as an indication of disease. This may at first sight appear to be a paradox, but under certain circumstances a minute haemorrhage may be the earliest sign of the development of a serious disease, while a copious haemorrhage resulting from a trifling breach of surface may prove to be of no importance beyond the temporary effect of the loss of blood, which is soon made up again. It will be realized, therefore, how important the subject is, and how difficult it is in some cases to estimate the full significance of an unexpected haemorrhage. When in doubt it is certainly better to over-estimate the importance of this symptom and treat it accordingly than to under-estimate it and treat it lightly. The investigation of a case of haemorrhage may tax all our experience and resources, but the diagnosis of the true cause is a question of the greatest interest, which may well call into play our best powers of observation. In the time at our disposal we cannot consider all the possible causes of haemorrhage in disease. Many of the common causes of haemorrhage are so well known that I shall only consider some forms of haemorrhage and the lessons that may be learnt from them.

In the first place let us consider the significance of bleeding from the nose. This is such a common event that even a sharp attack of epistaxis does not give rise to alarm unless it be unduly prolonged. In some persons it

is readily started by a very slight injury and in others it occurs from time to time without any apparent reason, and careful examination may reveal no nasal disease to account for it. There are, of course, many local nasal diseases which may be accompanied by epistaxis, but to these I shall not refer further. When epistaxis occurs with fever it may be an early symptom of enteric fever, especially if it is associated with frontal headache.

As an example of unexpected epistaxis in association with another infection, the following case, which I saw with Dr. Surridge, is of interest:

A lady, aged 47, had been taken ill a week before with fever; the temperature at first was only 100°. On each of the last three evenings preceding the day of my visit the temperature had risen to 103°, and there had been recurring attacks of epistaxis. The only two symptoms were the fever and the epistaxis. The latter had not been sufficient to require special means to check it, as the patient felt relieved by each loss of blood. This association of symptoms at first suggested the onset of enteric fever, especially as some little time before there had been a limited epidemic of typhoid fever in the neighbourhood. The spleen, however, was not enlarged; there was no distension of the abdomen; there were no rose-coloured spots, and the Widal reaction was negative. It was ascertained that there had been a fair number of cases of influenza in the district, and that in several cases fever and epistaxis were the only symptoms. We came to the conclusion, therefore, that this was a case of influenza with epistaxis. The epistaxis did not recur, and after several days the temperature became normal without the development of any other symptoms. Influenza is a curious disease, in that the symptoms vary in different epidemics and in different districts. Thus, in one area the disease may be mainly characterized by bronchitis and bronchopneumonia, in another by gastro-intestinal catarrh, or, as in this case, by epistaxis, though this is not a very common event.

The occurrence of epistaxis in granular kidney and arterio-sclerosis is well known. A sudden attack of epistaxis occurring in a man who has passed middle age may be the first indication that he is suffering from granular kidney. This symptom naturally leads us to examine the urine, take the blood pressure, and make an ophthalmoscopic examination. It is remarkable how advanced a stage of the disease we may find to be present in a patient who comes first under observation for an attack of epistaxis.

The importance of haemoptysis is well known, and by far the commonest cause is pulmonary tuberculosis; it may be the earliest symptom to attract attention. Any haemorrhage from the lungs should naturally lead us to suspect pulmonary tuberculosis and take every pains to ascertain if it is present. An aneurysm or new growth in the lung or a pulmonary infarction may all cause a spitting of blood. Errors, however, may arise from various causes. Dr. Bramwell, in his Address in Medicine at the Annual Meeting of the British Medical Association at Birmingham, gave an illustration of how the haemoptysis which occurs in association with mitral stenosis may lead to a wrong conclusion as to its cause if the chest is not thoroughly examined. Bronchial haemorrhage may be brisk and yet never recur. I remember one case in a man, a butler by occupation, who had a profuse haemoptysis, in whom there were no physical signs. The haemorrhage, I believe, never recurred, and no other symptoms developed, and certainly more than ten years afterwards he was well and in a situation. This case was an example of haemorrhage from the bronchial mucous membrane allied to some forms of epistaxis and to gastrostaxis as described by Dr. Hale White.

In another case, a young man, a personal friend of my own, had some slight haemoptysis, which we concluded at the time came from the lungs. He had an attack again when staying in Ireland, and a laryngoscopic examination, which was made by the physician who saw him at the time, revealed the fact that the blood came from a dilated vein in the glosso-epiglottic fold, which was actually bleeding at the time of the examination. I afterwards saw the vein myself, but never when it was bleeding. This is now many years ago, and the patient is in excellent health. Haemorrhage from the gums may sometimes be

mistaken for haemoptysis, as in a case mentioned by Dr. William Murray in his *Rough Notes on Remedies*.

When blood is passed with the urine it may come from any part of the urinary tract, from the kidney down to the urethra. Generally speaking, we have to distinguish blood which comes from the kidney or its pelvis from that which comes from the bladder or prostate. When blood comes from the kidney it is uniformly distributed through the urine. If small in amount it may make the urine "smoky," and there may be the "beef-tea" deposit; if abundant it may impart a bright red colour to the urine. Blood which comes from the bladder or prostate appears chiefly at the end of micturition, as may be demonstrated by getting the patient to micturate into three different glasses in succession. Haematuria may occur in tuberculosis of the kidney and in the early stages of a new growth of the kidney, and may be produced also by the presence of a renal calculus. It may occur also in acute Bright's disease and in chronic granular kidney; in the former case the cause is generally obvious. A profuse attack of haematuria should always lead to a careful examination of the urine, the blood pressure, and the heart, to ascertain whether there is any evidence of a chronic granular kidney.

Apart from these well-known causes, I wish to draw attention to cases in which a sharp attack of haematuria proves to be of no importance, and, on the other hand, to some cases in which a trifling attack is in reality an early indication of the presence of serious renal or vesical disease. There is an interesting form of haematuria which occurs apart from any organic disease; it is known as "essential renal haematuria," and has been described by Senator, and recently in this country by Dr. Hale White. In this disease recurring attacks of haematuria take place. In some cases the loss of blood has been sufficient to endanger life, though it is rarely fatal. In cases in which an operation has been performed, the kidney has been found to be quite healthy, and, curiously enough, in some the attacks have ceased after a simple nephrectomy. In some cases presenting similar clinical features the haemorrhage has proved to be due to an angioma of a renal papilla, but these, of course, are not cases of "essential renal haematuria" and require a nephrectomy to remove the source of the haemorrhage. There is, however, another variety of haematuria in which a single attack, or two or three attacks, of haematuria occur close together, without subsequent recurrence. These may be termed examples of accidental haematuria. These cases are apt to give rise to a good deal of anxiety at the time, as the loss of blood may be considerable. The absence of subsequent recurrences during a long period of years of good health shows clearly that in these cases there is no structural change in the kidney. Two personal friends of my own, one a physician and the other a surgeon, each had such an attack a good many years ago. I saw each of them at the time, and in both cases we could find no cause for the haematuria. It ceased within a few days, and has not, as far as I know, recurred, and both are in good health. In another case the haematuria was induced by a sudden chilling of the surface of the body by bathing in cold water when heated by exercise. A clergyman, while on a holiday in the Lake District in the month of August, took a long walk, and as he felt very hot he bathed in a mountain stream. After doing this he twice passed red urine, which evidently contained blood. He had another similar attack on his return home after a walk, and his medical adviser said that the urine contained blood. He was told at the time that the haematuria was due to a renal calculus. When I saw him I ascertained that he had never had any renal colic, and there was no pain or tenderness on pressure in either renal region. There was no frequency in micturition and the urine was normal. I came to the conclusion that it was a case of accidental haematuria. This opinion was evidently correct, as I happened to meet him some years afterwards and he told me he had had no return of the symptoms.

In some cases a trifling form of haematuria may on further investigation prove to be an early indication of definite disease, as is well illustrated by the two following cases. A young lady, aged 18, a month before I saw her had strained herself and felt some pain in the lower part of the abdomen. On several occasions she had passed a

few drops of blood at the end of micturition. A week previously she had again had pain and passed blood, but had felt no pain since. The left kidney was found to be movable, but it was not tender on moving it nor on grasping it between the two hands. She had some pain two days later. No further symptoms were noticed until some two months had elapsed, when she again passed a few drops of blood. She was requested to send the urine next time any bleeding occurred. Five months after the first attack she had a slight loss of blood as at the beginning for three days, and sent me a sample of the urine. On looking at this with the naked eye a small particle was visible floating in the urine. This was at once examined under the microscope, and was seen to be a small portion of a papilloma. I sent the patient to the late Professor Annandale, of Edinburgh, who wrote to me as follows:

"I put Miss A. under chloroform and made a cystoscopic examination of her bladder. Our diagnosis was confirmed, and I found a well-marked villous growth at the lower and posterior wall. The urethra was so readily dilatable that I was able to introduce my finger into the bladder and still further confirm the diagnosis, and also determine that the growth had a diameter of about a shilling, was quite superficial, and did not infiltrate the submucous tissues. It could easily be reached by the finger, and accordingly I scraped it away, partly by the finger nail and partly by a sharp spoon, and then by means of a lithotripsy evacuator washed out the fragments. This allowed me to collect all the debris, which consisted entirely of villi, rounded in shape and soft in consistence." Microscopical examination showed that the growth was a typical papilloma of the bladder in a very early stage.

I mention this case because, although there had been several haemorrhages, the quantity of blood lost on each occasion only amounted to a few drops, and it was remarkable that a recognizable portion of the growth should be found at that stage in the first sample of urine examined microscopically.

The next case I wish to refer to also furnishes an illustration of how an immediate microscopic examination of a fresh sample of urine may supply information of the greatest value in determining the source of an obscure case of haematuria.

The case was that of a boy aged 16½, who, in December, 1911, was brought to see me by Dr. W. Turner, to whom I am indebted for the history of the case. The patient was born in Pondoland, S.A., and lived there until he was 12 years old. Subsequently he had resided in England, and the matron of the school to which he was sent informed his grandparents that she had frequently noticed what appeared to be the presence of some kind of discharge on the underclothing. During the summer of 1911, when the boy was 16 years old and had resided in England for four years, he became ill. He was noticed to be heavy and dull, especially after exertion or waiting longer than usual for his meals. The appetite was voracious, and he had frequent attacks of biliousness. He looked ill, the complexion was muddy, and the eyelids puffy. Physical examination revealed no abnormality in either chest or abdomen. The urine was found to be alkaline and of low specific gravity, and to contain albumin and red blood corpuscles, but no pus cells and no casts.

In September the Clinical Research Association examined the urine, with the following result: Reaction, slightly alkaline. Specific gravity, 1013. Albumin, fair amount. The centrifugized deposit contained many red blood corpuscles and a few triple-phosphate crystals, but no tube casts, pus, renal epithelium, or other urinary abnormalities. Further examination by Dr. Almond of the urine in October showed the presence of red blood corpuscles, pus, and epithelial cells.

Early in December his general health was excellent, and he had lost his lassitude. He only complained of his sight becoming rather less distinct after reading for any length of time. The optic discs were normal. The systolic blood pressure was 121 mm., and the diastolic pressure 80 mm. The centrifugized deposit of the urine contained a few red blood corpuscles and many pus cells, a few granular casts, a few oxalate crystals, and epithelial debris. At the end of December, when Dr. Turner brought him to see me, he was passing in the urine small masses of what appeared to be red blood clots. When I saw him there was nothing abnormal to be found on physical examination. We got the boy to pass a fresh sample of urine, in which with the naked eye a small pinkish mass could be seen floating. This was mounted at

once on a glass slide and examined under the microscope, when I found it was a small fresh clot of blood, in which were entangled some ova of the *Bilharzia haematobia*. This examination at once showed the true nature of a puzzling case, and clearly indicated that the boy was suffering from bilharziosis, which he had contracted in Pondoland at least five years before.

In connexion with renal disease I wish to allude to the significance of retinal haemorrhage. In this connexion also, although the amount of blood which actually escapes from the retinal vessels is very small, the significance is great, indicating an advanced stage of renal disease, and is of ill omen.

Gastro-intestinal haemorrhages are in some cases very difficult to explain. Apart from bleeding due to actual ulceration, we are familiar with haematemesis, which occurs in the early stages of splenic anaemia or from the rupture of an oesophageal varix in cases of alcoholic cirrhosis of the liver. Stadelmann¹ has recently shown that some cases of obscure gastro-intestinal haemorrhage are due to the rupture of idiopathic varicose veins which may occur in the stomach, in the small intestine, and in the rectum. Dr. Hale White has drawn attention to a special form of bleeding from the stomach which he has named gastrostaxis. In this condition when the stomach has been opened at an operation the blood has been found to be oozing from an area of congested mucous membrane. Dr. White² has suggested that such haemorrhages may be due to injury of the vessels in the mucous membrane by an endothelial toxin.

I wish in passing to call attention to the very profound secondary anaemia and prolonged ill-health which arises in some cases from small repeated haemorrhages, of almost daily occurrence, from haemorrhoids; the haemorrhage has been neglected by the patient and allowed to go on unchecked for years before medical advice is sought. In these cases the haemorrhage is not of importance as an indication of disease nor on account of the amount lost on any single occasion. It is the repeated small losses which impose so great a strain upon the blood-forming organs that a profound secondary anaemia results. The occurrence of these haemorrhages is not mentioned by the patient, perhaps from feelings of diffidence, and it is astonishing how long they are tolerated without complaint.

I have not spoken at all of haemorrhages arising in haemophilia, purpura, and allied diseases. These are generally recognized, and it is not necessary for me to do more than mention them. I have dealt only with a few aspects of what is a large and important subject, and one of general interest, and time will not permit me to go into the question of treatment, as my object has been to direct attention to the importance of arriving at a correct diagnosis in every case of obscure haemorrhage, so that the right treatment may be applied.

REFERENCES.

¹ *Berl. klin. Woch.*, May 5th, 1913; *BRITISH MEDICAL JOURNAL*, Epitome, October 18th, 1913. ² *Lancet*, February 17th, 1912.

THE Khedive has founded a special hospital at Alexandria for the radical cure of hernia. The hospital will be housed in a pavilion of the great institution known as the Abbassi Asylum. It is to be called the Abbas II Hospital, and is to be under the surgical direction of Dr. Colloridi Bey.

A SCHOOL for health officers has recently been organized in connexion with Harvard University and the Massachusetts Institute of Technology. The organization of this school marks, it is said, a distinct epoch in the American Public Health Service. By the co-operation of the two institutions it will be possible for properly qualified persons, on payment of an annual fee of £50, to be admitted to all the resources of the Harvard Medical School and other departments of that university, as well as to the chemical, biological, sanitary, and engineering opportunities offered by a great modern technical school. No degree will be awarded on the completion of the course, but a certificate of public health (C.P.H.) will be given to all who go through the course satisfactorily. No degree is required for admission, but no one will be admitted who has not completed at least two years of ordinary college work, including chemistry, physics, biology, and French and German, or who is not otherwise specially qualified. Professor M. J. Rosenau of the Harvard Medical School is the Director.

A Lecture

ON

THE EARLY DIAGNOSIS AND OPERATIVE
TREATMENT OF CARCINOMA OF
THE CERVIX.

DELIVERED AT THE CANCER HOSPITAL, BROMPTON.

BY

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IN my work at this hospital I have been struck by the hopelessly advanced stage of the disease in many of the patients who have applied for treatment of carcinoma of the cervix for the first time, and in the ordinary methods of dealing with it there seems to be a lack of the thoroughness and cleanness of dissection which have been applied with such success to the eradication of cancer in other more exposed and accessible organs, such as the breast and the tongue. It is therefore to the great importance of early and accurate diagnosis, and to modern lines of treatment, that I chiefly wish to direct your attention.

The cervix may be divided into:

1. That part which lies free within the cavity of the vagina and is covered with the stratified squamous epithelium of the vaginal mucous membrane.
2. The supravaginal portion, which lies embedded in the lowest portion of the pelvis in the mass of loose connective tissue called the parametrium.

This anatomical classification forms a very useful basis in discussing carcinoma. For the disease beginning in these two portions not only differs in its pathological characters, both macroscopic and microscopic, but also in its zone of spread, its liability to infect the neighbouring lymphatic glands, and, I think, to a certain extent also in its ultimate prognosis.

CLINICAL TYPES AND THEIR METHOD OF SPREAD.

Carcinoma arising from the free surface of the cervix grows partly outwards as an exuberant proliferating mass, partly downwards into the fibro-muscular stroma as long branching columns of atypical epithelial cells. Depending upon which of these two modes of growth is the more obvious, certain clinical pictures result, and an intimate knowledge of their appearances is essential for accurate diagnosis. Upon the early onset or otherwise of fatty necrosis of the growth also depends the stage at which ulceration or the production of carcinomatous cavities is produced. At the same time it must be admitted that all these processes go on side by side, and it is by the predominance of any one of them that we are enabled to make use of the following arbitrary classification.

A. Carcinoma of the Vaginal Cervix.

1. *Papilliferous Form.*—Here a sessile protuberant growth projects from one or both lips of the cervix into the cavity of the vagina. The specimen I show you here more closely resembles one of those beautiful villous tumours of the bladder than anything else. This, however, is exceptional. The surface of the growth is usually concealed by a yellow sloughy mass, bathed in a pool of mucus.

2. *Infiltrating Form.*—Here the cervix is enlarged and becomes a cartilaginously hard, shapeless mass, with usually a certain amount of superficial ulceration of the overlying mucous membrane. On section, it is seen to be occupied by an opaque white growth.

3. *Ulcerative Form.*—Here the disease may show itself either as (a) a shallow ulcer tending to spread outwards on to the vaginal vault, with little infiltration of the underlying tissue; or (b) a crateriform cavity with hard everted edges occupying the former position of the cervix, the vaginal portion of which may have completely disappeared.

Methods of Spread.

Carcinoma of the exposed portion of the cervix tends to spread downwards into the vagina, and outwards into the lowest portion of the parametrium. Although it