Section of Urology.

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Purpura of the Urinary Tract.

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ABSTRACT.—Twenty-four cases of purpura of the urinary tract are discussed and analysed.

Purpura of the kidney may be a cause of painless hæmaturia. In some cases nephrectomy may be necessary to check the bleeding.

Purpura of the bladder is a cause of painful hæmaturia. In such cases the diagnosis can be made with the cystoscope.

A number of the cases appear to be caused by a streptococcal infection of throat, teeth or bowel.

The exhibition of horse serum by the mouth usually has an immediate effect in checking the bleeding tendency.

Splenectomy should be considered in severe chronic recurrent cases.

Purpura is a symptom and not a disease. It can attack the kidney or bladder in any type of case. The attacks may be simple, recurrent or fulminating. In many cases no cause can be discovered, in others it is associated with acute rheumatism. In a number of cases a proximate cause can be discovered, in the nature of a bacterial infection, a chemical poison, a thrombocytopenia, splenomegaly, or the deprivation of some vitamin.

I HAVE chosen this subject for my address this evening, as I believe I share with Walsh the privilege of having first called attention to the cystoscopic appearances of purpura of the bladder, though it is clear that Blum had also recognized the condition independently, and I believe I was the first to describe the appearance of purpura in a kidney removed for profuse hæmaturia. Since my first observation in 1910 I have observed a number of instances of the affection, a description of which I shall bring before you.

In 1910 a girl was admitted under my care at the London Hospital, suffering from profuse hæmaturia. Immediate cystoscopy revealed numerous petechiæ scattered throughout the mucous membrane of the bladder. I made a diagnosis of "Purpura of the Bladder," and described the case and the cystoscopic picture in the *Annals of Surgery* in September, 1913. In the *American Journal of Surgery* for September, 1913, p. 332, F. C. Walsh published a fatal case of "purpura hæmorrhagica," in which he described a similar cystoscopic picture, his case having been observed for the first time in January, 1913. In 1914, Bruni [1] published a third case of purpura of the bladder, observed with the cystoscope, and in his case, petechiæ were also to be observed in the skin. In 1914, Blum [2] gave a general description of the condition with which he said he had been familiar for some years, and published a coloured picture of the cystoscopic appearances of purpura of the bladder, stating, however, that the condition was likely to lead to ulceration, a point in which most future observers, except Szabó [3], have not been able to follow him. The question of priority has since been discussed by Denicke [4], Farago [5], Kretschmer [6] and Praetorius [7]. Further cases were described by Nelson, 1914 [8], Perrier, 1917 [9] and Kretschmer, 1918 [6]. In 1919, Stevens and Peters [10] described twenty-six cases which they encountered during the examination of 204 consecutive cases labelled "trench nephritis," admitted to a base hospital in France during the war. Since then the condition appears to have been noticed by a certain number of urologists, but does not appear to have received the wide recognition that it deserves. Lack of space forbids a full list of references to purpura in general, some 300 of which, up to 1924, have been obtained for me by the courtesy of the American College of Surgeons.

C. J. G. Taylor and Professor Turnbull [11], of the London Hospital, describing the post-mortem appearances of a fatal case of purpura, mention the occurrence of petechiæ in

the mucous membrane of the kidneys and bladder. In 1916, I observed for the first time purpuric lesions of the pelvic mucous membrane in a kidney removed at operation, and since then I have removed six similar kidneys. I published this case on p. 287 of my book "Common Infections of the Kidney" (1920), and discussed the question of purpura of both bladder and kidneys fully (pp. 145-149). Arnold Schwyzer [12] described four cases of "essential hæmaturia," and in Case 4 he noted that the mucosa of the renal pelvis showed rather numerous minute hæmorrhagic spots, but he seems to have missed their true significance. Praetorius [7], in 1924, described three cases of purpura of the kidney, his first case having been observed in 1920, and ventured the opinion that these were the first cases of purpura of the kidney to be described and published. Stephen Mackenzie [13] collected 200 consecutive cases of purpura out of 63,000 consecutive cases entering the medical wards of the London Hospital, stating that the disease appeared to be rare. Since 1912 I have met with a considerable number of cases, and have analysed for the purposes of this address twenty-four proved cases of purpura of the urinary tract, so that the condition is more common than Mackenzie's figures suggest, probably because many of the cases are ambulatory and are not admitted to the wards, or have escaped recognition there.

Purpura is characterized by the appearance of spontaneous extravasations of blood into the skin, mucous membranes, joints, retinæ and interstitial tissues. The resulting lesions in skin or mucous membrane are called petechiæ. Petechiæ are blood-red or purple spots and patches which may be rounded, ovoid, linear or irregular in shape, and vary in size from that of a pin's-head to patches nearly half an inch in diameter. Occasionally they assume the character of large bruises or even hæmatomata. They do not disappear on pressure, but in a few days they turn brown and then fade away altogether. Hæmorrhages can also be observed in the interstitial tissues of the viscera in cases of purpura or "the hæmorrhagic disease" as it is often called.

That hæmaturia was of common occurrence in cases of purpura has been recognized for many years, but it is remarkable that petechiæ of the bladder should have escaped recognition by cystoscopists for so long.

I have included in these twenty-four cases only those where it has been possible to prove the condition to be one of purpura. All of them came up as cases of hæmaturia for diagnosis of the possible cause. Many of them presented petechiæ on the skin. The majority of them presented petechiæ in the bladder as viewed by the cystoscope. Some of them showed petechiæ in the mucous membrane of kidneys removed for dangerous hæmaturia. Some presented joint swellings, presumably due to extravasation of blood into the joints. Others had bleedings from the bowel, nose or teeth, and one had nephritis. During the same period I have met with a number of cases of hæmaturia where the bleeding observed to come from one or both kidneys has cleared up, and where the clinical course has suggested that the condition was one of purpura of the kidney. As in such cases absolute proof has not been possible they have not been included in the analysis. But I feel sure that such cases of purpuric bleeding from the kidney are not uncommon and explain many cases of painless hæmaturia. A purpuric bladder is always painful but a purpuric kidney usually causes no pain.

The observations suggest that cases of purpura of the urinary tract can be roughly classified into three main clinical groups:—

(1) *Purpura simplex*, which exhibits a single or a few mild attacks of hæmaturia, which soon clear up and are not thereafter repeated.

(2) *Purpura recurrens*, which exhibits repeated severe attacks over a period of years and which may gradually react to treatment.

(3) *Purpura fulminans*, where one or two severe attacks appear within a short time of one another and rapidly lead to the death of the patient within a few weeks or months.

They can be also divided clinically into:—

(1) Purpura of the bladder with painful hæmaturia.

(2) Purpura of the kidney with painless hæmaturia.

The meaning of these groups can be most readily appreciated by the recital of illustrative cases:—

Case 1.—*Purpura Simplex. Purpura of the Bladder.*

A girl, aged 12, admitted to the London Hospital on November 30, 1910, stated that on the evening of November 28 she felt a sudden desire to pass water, and during the act experienced a sharp stabbing pain, starting in the left iliac region and spreading into the vulva. Between 8 p.m. and 9.30 p.m. she passed

water four times, each time noticing a similar pain, which lasted only as long as water was passing, and ceased at once at the end of the act. At 9.30 p.m. she passed water again, and this time inspected it. It wa· full of blood. An aching pain came on in the left iliac region when she went to bed, and lasted all night and the whole of the next day. Urine was passed once in the night and five times during the next day until the time of admission into the hospital at 5 p.m. on November 30.

Previous Health and Habits. Diphtheria five years ago, otherwise no serious illnesses. No hæmophilia, no scurvy. The patient lives in Poplar amongst poor and unhealthy surroundings. She has had a sore throat for some days before the onset of the hæmaturia, and has felt "out of sorts."

Examination.—The patient looks ill, and is pale and anæmic. The temperature is normal, pulse and respiration rate are normal, the tongue clean and moist, the heart, lungs and alimentary system normal. There is follicular tonsillitis on the left side, and some slight enlargement of the glands on the left side of the neck which are tender to the touch. The skin shows no petechiæ, and the gums are healthy. There is deep tenderness over the bladder region, especially on the left side. The urine is full of blood-clots, and contains bright red blood diffused throughout.

The patient was at once taken into hospital and put to bed. By the next morning the bleeding had ceased, and the pain had disappeared.

December 1, 1910.—X-ray examination of bladder and kidney areas shows an absence of stone shadows. The urine is clear to the naked eye, 38 oz. in twenty-four hours, the reaction acid, specific gravity = 1021, no albumin, urea 2·5 per cent. Hæmo-renal index (electrical resistance of urine and serum) = 1·5 (normal 2).

December 2, 1910.—*Cystoscopy.*—The bladder was filled with 8 oz. of oxycyanide of mercury solution 1 in 4,000. Both ureters appeared healthy. The bladder wall for the greater part appeared pale and healthy, but scattered irregularly over fundus and trigone were seen patches of submucous hæmorrhages varying in size from a pin's head to a sixpence. The patches were of all shapes and sizes, some linear, some stellate. The greater number were scattered over the fundus. There was no ulceration and no sign of miliary tubercles. I came to the conclusion that I was either dealing with a purpuric condition of the bladder wall, or that I had caught a primary blood infection of tuberculosis at its very onset.

On December 5 and again on December 6 a twenty-four hour specimen of urine was examined for tubercle bacilli and for pus cells—none were found.

A "von Pirquet" tuberculin reaction was done and was positive

The urine remained clear until December 9, when another attack of pain and bleeding came on exactly similar to the first one. This lasted two days and then cleared up completely. Throughout the whole time the patient was in hospital the temperature remained normal, and there were no signs o constitutional disturbance except that the patient felt below par.

December 15, 1910.—*Cystoscopy.*—No pain, no increased frequency, no blood for four days. The picture has changed completely, the bladder is quite healthy again except for faint patches like fading bruises on the wall of the fundus. There is also a small fading hæmorrhagic patch about an inch above the middle of the bar of Mercier, into which a small blood-vessel is seen to run and be lost.

December 16, 1910.—*Blood Examination.*—Coagulation time—five minutes. Red blood-corpuscles 5,000,000. Hæmoglobin 85 per cent. Colour index 0·8. White cells in normal proportions

Course.—Calcium lactate 10 gr. three times a day were administered for a week, and the patient left the hospital on December 19 restored to health, and has since had no return of the bleeding.

Case 2.—*Purpura Simplex. Purpura of the Kidney.*

A woman, aged 38, was admitted under my care at the London Hospital on December 18, 1916. She stated that three weeks previously she developed active incontinence of urine and strangury. Six weeks later the strangury suddenly ceased and she began to pass large quantities of blood in her urine. This had continued on and off ever since.

The patient appeared wasted and anæmic, but exhibited no physical signs. The urine contained a large quantity of blood and numerous coliform bacilli in pure culture, but no pus or casts. The blood showed no changes except those of secondary anæmia. Cystoscopy revealed blood pouring out of the right ureter in cascades. The urine from the left kidney was natural. X-ray examination was negative.

On December 19, 1916, the right kidney was removed as an early tumour was suspected. Examination of the kidney showed large purpuric spots and patches under the mucous membrane of the pelvis. No other changes could be discovered, except slight degeneration of the cells of the collecting tubules.

This case was described in my book, "Common Infections of the Kidney," 1920, p. 287.

Case 3.—*Purpura Recurrens. Purpura of the Kidney and Bladder.*

A single woman, aged 40, was examined in May, 1925. Her doctor stated that in June, 1924, she suffered from strangury, pain in left kidney and bacteriuria, and in November, 1924, had a second attack. Since January, 1925, there has been increased frequency, pain on passing water and constant aching pain in left kidney. For the last six weeks she has been confined to bed with slight fever 99·5° F., profuse sweating, and daily growing more ill and anæmic. No pus or bacteria could ever be found in urine. Recently she has had profuse hæmaturia, which led her doctor to call for further advice.

On examination the left kidney was felt to be considerably enlarged and tender, and the urine full of blood. X-ray examination was negative for stone.

On May 27, under ether anæsthesia cystoscopy showed that the bladder mucous membrane was covered with large purpuric patches. In between the mucous membrane was healthy. Blood was pouring in cascades from the left ureter. A specimen obtained by catheter from the right kidney was natural and of good functional value. As the bleeding seemed grave and increasing in severity day by day it was decided to remove the left kidney.

On opening the kidney after its removal it was found to contain a large number of purpuric spots and patches beneath the pelvic mucous membrane. No other pathological changes could be found.

The patient was given three doses of 25 c.c. of antistreptococcic serum by the mouth at intervals of forty-eight hours.

Recovery was uneventful and the patient appeared to regain her usual state of health.

There was no further trouble until October, 1925; then for a week she had slight fever, and two attacks of slight hæmaturia and increased frequency. She was given three doses of antistreptococcic serum by the mouth. The bleeding at once stopped.

The teeth were X-rayed, and five or six dead stumps noted, but their removal was refused. The urine and fæces were examined by Dr. Fleming. He found a hæmolytic streptococcus in the stools and a strain of *B. coli*, which the blood agglutinated in high dilutions. Autogenous vaccines were started. *The first dose produced a severe attack of hæmaturia.*

October 19, 1925.—*Cystoscopy.*—The bladder was full of clots, which had to be washed clear. Several large and many small purpuric patches could be seen on the base of bladder. One was abraded and bleeding. It was advised that she should go on with vaccines but in smaller doses, to take calcium lactate from time to time, and to have three doses of antistreptococcic serum by the mouth if she were to bleed.

January 28, 1926.—She has had the vaccine once a week regularly, and the bleeding has stopped completely.

Before the vaccines were started coli agglutination of serum was 1/500; now it is 1/2500. No agglutination of streptococci. Opsonic index to streptococcus 1·34.

Her general health has greatly improved, she has no fever, and is able to get about. If more than ½ c.c. of vaccine is given, she gets a reaction in the bladder, accompanied by hæmaturia. She was again advised to have the teeth removed.

August 4, 1926.—She has been wonderfully well. Six dead teeth have been extracted. There has been no hæmorrhage since then till this week. She is putting on weight, and looks quite fit again. She has had 1/5th c.c. of vaccine regularly once a fortnight. Last week a drop of blood on napkins. Cystoscopy — four or five tiny purpuric spots seen just at entrance to urethra on the trigone.

February 24, 1927.—She has been the picture of health, and has had the vaccine regularly. During the last few days she has noticed a few drops of blood on her napkins, and slight pain in the urethra. The bladder appeared healthy except for a large purpuric patch on the trigone, just at the entrance to the urethra. Three more doses of serum given.

March 17, 1928.—She writes to say she considers that she is completely cured, as she has had no more trouble and is in good health.

Note.—This was the only case out of eight with purpuric kidneys where pain was a feature. The remaining seven kidney purpuras had painless hæmaturia.

Case 4. *Purpura Simplex. Purpura of the Kidney.*

A married woman, aged 40, first examined in December, 1923, stated that for one week she had suffered from profuse but painless hæmaturia. The urine contained blood, but no pus, and was sterile. Cystoscopy showed that blood was pouring in cascades out of the right ureter. The efflux from the left ureter was clear, and the left kidney was of good functional value. A pyelogram of the right kidney showed a double pelvis, but no evidence of tumour. As the bleeding appeared to be endangering life, the right kidney was removed early in January, 1924. Examination revealed no pathological changes, except the presence of a number of purpuric spots scattered throughout the pelvic mucous membrane (see fig. 2).

Recovery was uneventful. The tonsils which were enlarged were removed. Since then there has been no further trouble of any kind, and in 1928 the patient is known to be in excellent health.

Case 5.—*Purpura Fulminans. Purpura of the Kidney.*

A man, aged 59, was first examined on August 16, 1921. His doctor stated that in May, 1918, the patient suffered from pain in the abdomen and diarrhœa. In May, 1921, he had a second attack accompanied by fever, and was in bed fourteen days. On July 14, 1921, he had pain in the pyloric end of stomach and fever, and had to go to bed, where he had been ever since. On August 3, 1921, he had an attack of retching and spat up blood *which came from the teeth.* That day he started *profuse hæmaturia.* This has persisted ever since, with no pain in bladder or kidneys, but with slight fever all the time. The urine is said to contain *B. coli* on culture. It contains a large quantity of blood, a few epithelial and blood-casts, but no pus. The temperature is never above 100° F. Calcium lactate has been given, acid. sod. phosphate, and later, alkalies and hamamelidis, but with no beneficial result.

On examination the patient looked weak and anæmic from loss of blood. The kidneys were not enlarged.

Cystoscopy showed the bladder-wall not inflamed, and blood pouring out of right ureter. The urine from the left kidney was clear and of good functional value. The gums were spongy and blue, and blood was weeping slowly from the margins round the teeth. There was a large subcutaneous hæmorrhage over the front of the right ankle. A provisional diagnosis of purpura was made, but as the pulse-rate varied between 70 and 90 per minute it was decided not to operate.

The patient was flooded with alkalies and given hæmoplastin. The urine on cultivation yielded the *Streptococcus fæcalis* and a Gram-negative bacillus (Lepper). Blood cultures were negative.

On the evening of August 17 the bleeding was more profuse and the patient was becoming blanched and restless, the pulse-rate having risen to 120 per minute. As it was obvious he was bleeding to death the right kidney was exposed. *The wall of the ureter was œdematous and glassy*, such as is often seen from irritation by blood. The ureter and pelvis were distended with blood, but there were no clots. The right kidney was removed. On opening the kidney the cause of the hæmorrhage was apparent. The pelvis of the kidney was covered with purpuric spots, some the size of a pin's head, some of medium size, and one quite a large submucous hæmorrhage in the middle of the pelvis. There were tiny white areas of fibrous tissue in the centre portions of the pyramids (see fig. 3).

Dr. Elizabeth Lepper very kindly examined the kidney while fresh, mounted it, and furnished a report which is given below (p. 25).

Progress.—There was considerable shock for twenty-four hours, but next day the urine was clear of blood, and the patient took a turn for the better. He was given hæmoplastin and alkalies.

August 21, 1921.—A bruise appeared on the left arm.

The wound healed on the ninth day, but continued to ooze a little blood-stained serum. Gastro-intestinal disturbances became more marked.

The patient went on fairly well until August 31, 1921, and had no more hæmaturia. Then acute delirium, rigidity and twitchings started suddenly. From this day on he got gradually worse. Though there was no return of any hæmorrhage, yet about the middle of September he gradually sank and died.

This case appears to represent a fulminating reaction to poisons absorbed from the teeth and alimentary canal.

The condition affected females more often than males (nineteen females to five males), and attacked young children (six), usually a mild type; or those well advanced into middle age (eighteen), the more serious type. Fourteen cases could be grouped as purpura simplex, eight as purpura recurrens, and two as purpura fulminans. In sixteen cases the purpura was confined to the bladder, in three cases it was present in both bladder and kidneys, in five cases it was confined to one of the kidneys.

Hæmaturia was present in all, was mild and transient in seven, was profuse and abundant, lasting for days at a time in ten cases, and was profuse, alarming and dangerous to life in eight cases, so profuse that nephrectomy had to be carried out. In the two fulminating cases nephrectomy stopped the hæmaturia, but the patients died of exhaustion or of hæmorrhage elsewhere in the course of a few months. In the other six cases nephrectomy stopped the hæmaturia and the patients' lives were saved. Of these, three had no further trouble of any kind and are in good health, one had trouble for a time but is now cured, two still suffer at times from mild attacks of hæmaturia.

Pain was a marked feature in all the bladder cases, an intense strangury felt at the neck of the bladder, accompanied by distressing frequency of micturition, often so severe as to make the patient cry out. In all such cases petechiæ were seen in the bladder mucous membrane.

In one case with severe recurrent purpuric bleedings from the bladder, one of the kidneys had been removed ten years previously by another surgeon for profuse hæmaturia, the cause being left unexplained. In another case I had to remove the right kidney for grave recurrent attacks of pyuria and hæmaturia due to *B. coli* in 1924. Two-and-a-half years later after a severe septic throat the patient was seized with strangury, hæmaturia, uræmic vomiting and purpuric bruisings in the skin. Cystoscopy revealed no cystitis but severe purpura of the bladdder, and profuse bleeding from the left ureter. The urine contained streptococci but no pus. The throat and teeth gave a pure culture of streptococci. Antistreptococcic serum at once relieved the condition. In five cases purpura attacked one of the kidneys only, the bladder being free from pain or petechiæ. In these the bleeding from one kidney was so profuse and alarming that the bleeding kidney had to be removed. The diagnosis was only made clear by finding petechiæ scattered over the pelvic mucous membrane of the excised kidneys, unaccompanied by any other demonstrable lesion.

Pain was not complained of in seven out of the eight cases diagnosed as renal. In this regard purpura of the kidney seems to differ from purpura of the bladder. In one renal case alone complaint was made of rather severe aching pain in the bleeding kidney, and in one other case the patient noticed a sudden sharp stabbing pain in one kidney just as the hæmorrhage started, which, however, disappeared in a few moments and did not return.

It would appear, therefore, that in only three out of twenty-four cases did petechiæ and hæmorrhage occur simultaneously in the bladder and in one or the other kidney. In only two cases did it occur in the second kidney after the first kidney had been removed for hæmorrhage. The cases where the trouble attacked the bladder were far less severe in type and did much better than those where it attacked one or both kidneys. The fact that petechiæ are likely to appear in bladder or kidney or both corresponds to the wayward nature of all purpuric lesions, bleeding and petechiæ appearing sometimes in the bowel, sometimes in the joints, sometimes under the skin, seldom in all situations in any one case, and usually sticking to the original site of predilection. In only one case was there evidence of a true nephritis, and in this case the nephritis was of a chronic type corresponding to the large white kidney or "nephrosis."

The blood in the urine showed little tendency to clot, so that there was no trouble from clots except in one child who had one attack of clot retention. This can be explained, as

though there appears to be little if any delay in the clotting time in cases of purpura, yet there may be a diminution in the number of blood-platelets, a lack of firm retractile fibrin in the clotted blood, and the bleeding time is usually prolonged (Hayem [14], Duke [15], Frank [16]). Exact observations of the blood were not made in a sufficient number of cases as to make it possible to classify the cases according to the blood changes. No case of thrombocytopenia (Frank [16]) was observed, but some may have been missed. In cases of suspected purpura elaborate examinations of the blood are needed and should include estimations of the blood-platelets, the clotting time, the bleeding time, and the nature of the retraction of the clot. The size of the spleen should be estimated by palpation and the X-rays. The application of the armlet of a sphygmomanometer at a pressure of 120 mm. of mercury to one of the arms for three minutes may produce a crop of purpuric spots in the skin of the arm and may be of diagnostic value (Tourniquet test of Hess).

Fever was absent in fifteen cases, and in the others there was only very mild fever, the temperature seldom rising to more than 100° F., despite the grave condition of some of the patients. In this respect the cases differ markedly from ordinary cases of pyelitis and cystitis, and resemble and are sometimes mistaken for acute rheumatism if the joints are swollen. In this respect they also differ from the cases described by Stevens and Peters, which appear to have been due to a peculiar type of poison related to the cause of trench nephritis.

Wasting was not noticeable except in four cases, *anæmia* was not profound save in eight cases. Fifteen cases were ambulatory and able to attend for examination in the clinic, and a number of these appeared remarkably well despite the strangury and hæmaturia.

In eight cases the patients were so desperately ill from loss of blood that it was necessary to perform nephrectomy, and in only two other cases did the patient's condition give cause for anxiety. In one the appendix was inflamed, and after its removal recovery ensued. In the other associated with fever and pyelitis, renal lavage quickly cured the condition.

The blood-pressure was usually low, possibly due to the loss of blood, a point which helps in the diagnosis from nephritis and congenital cystic kidney.

In two cases were noted intermittent painful swellings of the joints, in seven cases intermittent attacks of petechiæ or bruisings of the skin in various parts of the body, in four cases attacks of hæmorrhage from the bowel, and in two cases severe hæmorrhage from the gums. In these respects also they differed from the cases described by Stevens and Peters, wherein the lesions were confined to the bladder and kidneys.

Before increasing experience taught the lesson, the condition of the teeth and tonsils was not always noted, but as time went on it was recognized that herein were most likely to reside the cause of the trouble. In three cases in children purpura of the bladder came on shortly after the enucleation of tonsils containing pure cultures of streptococci, but no pus could be detected in the urine. In another case in a child the trouble came on the day after the extraction of a number of teeth infected with streptococci. In seven cases X-ray examination of the teeth revealed a number of septic stumps, the removal of which seemed to benefit the patients, and in four of these streptococci were isolated in pure culture from the teeth and the urine. In eight cases the tonsils appeared diseased and were removed, and in six of these streptococci were isolated in pure culture from the tonsils and urine. As regards the urine, there was usually a trace of albumin and an excess of epithelial cells in the centrifugalized deposit. A few blood and epithelial casts might be present, but granular casts in large numbers were absent except in one case that had chronic nephritis. In nine cases the urine was sterile, and in the majority of cases no pus was detected in the urine. In this respect again the cases differ from ordinary cystitis and pyelitis. Bacilli of the colon group were isolated in eight cases, usually without pyuria. In nine cases it was possible to isolate cultures of a streptococcus from the urine in the absence of pus, in two associated with bacilli of the colon group. It seems probable that by special methods streptococci would be more often isolated from these cases than has been possible in this series. Streptococci seem liable to die out in culture, or are apt to be overgrown by the bacilli of the colon group, unless special methods are adopted to encourage their growth.

More and more the impression was gained that a peculiar type of streptococcus was the most likely cause for the petechiæ, a streptococcus which might reside in the teeth, throat or bowel, and which by means of poison poured into the blood-stream might attack and injure the walls of the fine capillary blood-vessels so as to cause exudation of blood through them.

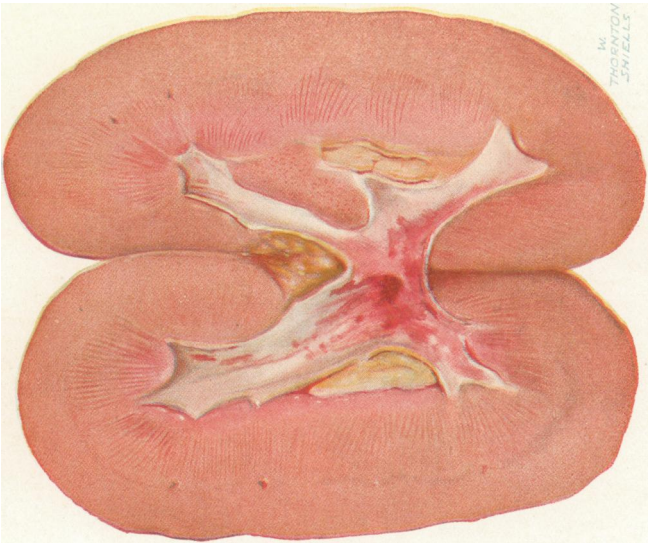

FIG. 3.

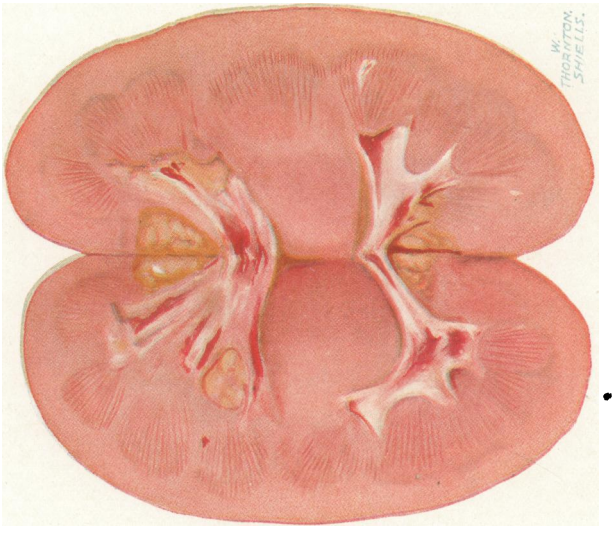

FIG. 2.

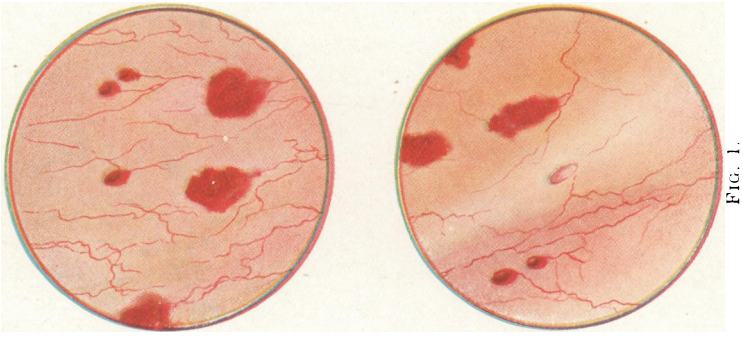

FIG. 1.

In two cases the injection of an autogenous streptococcal vaccine in too high a dose at once produced an attack of purpura and hæmaturia, and in one case this happened on more than one occasion.

In the majority of cases pus was absent from the urine, and in such cases the bladder mucous membrane as a whole did not appear inflamed, but was dotted over with petechiæ of varying shapes and sizes. In the cases where pyuria was present, all the blood-vessels of the bladder mucous membrane might appear very slightly injected, but the petechiæ stood out boldly and clearly even from the slightly reddened mucous membrane. In this respect the diagnosis from hæmorrhagic cystitis was usually quite distinctive.

During the same period I have met with five cases of sudden profuse hæmaturia caused by an acute solitary ulcer of the bladder ("Common Infections of the Kidney," pp. 139-145). I prefer to classify these as a separate group, but similar cases have been included under the group of purpura by Blum [2] and Szabó [3], who hold that a purpuric lesion of the bladder may either resolve or lead to necrosis with the formation of a "peptic" ulcer caused by the pepsin said to be present and active in acid urine. For this reason they recommend large doses of alkalies in all cases of suspected purpura of the bladder.

Description of the Cystoscopic Appearance of Purpura in the Bladder. (Fig. 1.)—(The blood-vessels seen in the bladder are veins, no arteries appear as in the retina.) In the majority of cases of purpura the mucous membrane of the bladder as a whole is normal or at most shows a very slight engorgement of the blood-vessels. Scattered over any portion petechiæ may be seen round, ovoid, linear or polymorphic and varying from the size of a pin's-head to patches half-an-inch or more in diameter. These patches may be scattered all over the bladder or be confined to one small area. In the case of pin-head petechiæ it is usually possible to trace a vein to its first visible tributary and perceive that the petechial spot lies just beyond the terminal portion of this. In other words, the petechiæ seem to be caused by an exudation of blood-stained fluid or blood into the tissues around a capillary blood-vessel just before it enters the finest veins (see fig. 1). The edges, though they may be irregular, are sharply defined and there is usually no inflammation around them. Large petechiæ may appear very slightly raised, but the mucous membrane over them is usually quite intact. In a few of the cases there could be seen mild diffuse submucous inflammation of the whole bladder wall, in the midst of which the petechiæ stood out boldly as blood-red spots and patches. It was in these cases that pus was present in the urine. If the bladder be examined a second time a few days later the spots can be seen to be fading, they are less well defined, more diffuse, and have assumed a brownish tinge. Examined a week or ten days later they will be found to have disappeared altogether.

Appearances met with in Purpura of the Kidney. (Figs. 2 and 3.)—On opening the kidney, the pelvic mucous membrane is found to be scattered over with purpuric spots, some as small as a pin's head, others larger, but there is no generalized engorgement of the blood-vessels caused by inflammation. The mucous membrane between the petechiæ appears pale and healthy. In one of the fulminating cases there was a large submucous hæmorrhage, which when fresh could be seen to ooze blood (see fig. 3, Case 5). Dr. Elizabeth Lepper very kindly cut sections of this kidney and reported :—

"The acute changes are almost limited to the mucous membrane covering the parietal wall of the pelvis; here the vessels are markedly dilated and full of polymorphonuclear leucocytes. There is a moderate round-cell infiltration of the submucous tissues and between the epithelial cells, and a very marked extravasation of red blood-corpuscles, which accounts for the naked-eye appearances and presumably for the hæmaturia, though in consecutive sections I have not been able to demonstrate any actual loss of epithelium exposing a vessel. There is slight leucocytic infiltration at the tips of the pyramids. The changes in the cortex are chronic in character, some patches of fibrosis being present. There is, however, cloudy swelling of the epithelium of the tubules. No organisms have been found in any of the sections. Cultures made from the fresh specimen and from the urine grew the *Streptococcus fæcalis*, and a bacillus of the proteus group."

There is no need to hypothecate ulceration of the mucous membrane. In all cases the blood appears to exude from the petechiæ, through the intact mucosa, as if continuously squeezed out of a sponge. It is extraordinary to observe how much blood may thus flow away in the urine merely by transudation, without ulceration or breach of surface.

In another case (fig. 2, Case 4), where the kidney had to be removed, Dr. Cavendish Fletcher reported:—

"The mucosa of the pelvis and calyces is studded with small hæmorrhages. Sections have been cut from various parts and show small areas of extravasated blood just beneath the epithelium of the renal pelvic mucosa. *Similar areas are also evident in between the collecting tubules in various places.* No other pathological changes could be found. The condition is presumably a purpuric one."

There seems then to be sufficient evidence that "purpura," whatever its cause, may involve the bladder mucous membrane when the petechiæ can be seen with the cystoscope, or involve the mucous membrane of the pelvis of the kidney when the petechiæ can be observed and examined microscopically after the removal of a kidney for grave hæmorrhage. These changes can be observed in a number of cases where other purpuric lesions are present in other parts of the body, such as the skin, the bowel, the joints and the teeth, or they may occur in cases where the petechiæ are entirely confined to the urinary tract.

One of the most striking features is that quantities of blood can be lost, so large as to render the patient exsanguine and blanched, yet the purpuric lesions found in the kidney may seem comparatively small. The blood must ooze continuously from the petechiæ owing to the prolonged bleeding time.

In none of the cases was the ophthalmoscope used. Stephen Mackenzie [13] mentions that petechiæ can be seen in the retina with the ophthalmoscope in some cases of purpura, but they are of rare occurrence. Senator and Litten [17] mention retinal hæmorrhages in their text-book, published in 1905. Otherwise, I can find no reference in the literature to petechiæ of the retina until Moreland McCrea [18] published a description of fifteen such cases, with coloured drawings of the lesions, drawings which correspond closely in appearance to petechiæ as observed in the bladder with the cystoscope, save that no arteries are visible in the bladder, but simply veins. In all his cases McCrea detected areas of focal sepsis. Rapid improvement of vision followed the treatment of these foci in ten of the cases. Recurrence of the petechiæ took place in three cases attended by recurrence of focal sepsis.

SUMMARY.

Purpura of the urinary tract appears in two clinical guises:—

(1) *Vesical*, with sudden onset of profuse painful hæmaturia, but with little or no systemic disturbance. The diagnosis can be readily made by immediate cystoscopy, and the prognosis is good.

(2) *Renal*, with sudden onset of profuse painless hæmaturia and little symptomatic disturbance apart from severe loss of blood. The cystoscope reveals blood pouring from one or both kidneys. Pyelograms are normal. The diagnosis is made in some cases by nephrectomy, in others by the presence of purpura elsewhere in the body, by the examination of the blood, or by the tourniquet test. In many cases the diagnosis can only be provisional.

Diagnosis.—For a long time it has been the custom in urological circles to talk of "essential hæmaturia." I prefer to class all cases so labelled as "cases of hæmaturia of which the cause has not been determined." The term "essential hæmaturia" begs the question and obstructs research. I believe that a number of the cases usually labelled essential hæmaturia are in reality cases of purpura of the kidney, that purpura is not at all an uncommon cause of hæmaturia from the bladder or the kidneys, and that its nature is missed either because cystoscopy is not carried out at an early period when petechiæ could be observed in the bladder, or because where pain and petechiæ in the bladder are absent, there is usually no occasion to remove one kidney, and so the probable purpuric nature of a bleeding kidney cannot be determined by direct observation. In all cases of unexplained hæmaturia a rigid examination of the skin, joints, retinæ and the hæmopoietic system may reveal the true nature of the case. It is the rule for the patient completely to have failed to notice or to exhibit unasked even quite large petechiæ on the skin, so that these need to be specially looked for. The diagnosis can be made readily if cystoscopy be carried out within a day or two of the bleeding and if the bladder is then seen to be covered by petechiæ. In these cases the hæmaturia is painful. It can be put forward provisionally if an early cystoscopy reveals a profuse bleeding from one kidney, and if a pyelogram shows a perfectly normal outline to the pelvis of that kidney, neoplasm being thus excluded. In these cases

the hæmaturia is usually painless. If the blood be examined and shows a marked diminution or absence of platelets, prolonged bleeding time, normal clotting time, or the presence of a characteristic non-retractile fibrin in the clot, then the diagnosis of thrombocytopenia purpura can be confidently made. If petechiæ are observed in other parts of the body, the diagnosis is at once apparent. The static resistance test of Hess may throw light on the diagnosis. A tourniquet is applied for three minutes to one arm. In cases of purpura this should produce purpuric spots on the skin of the arm. Even so, a large number of cases must remain not proven, but if it is once recognized that painless purpuric bleeding from one or both kidneys is not uncommon, then the minds of urologists will be set at rest and they will not be in too great a hurry to remove a bleeding kidney less they miss an early neoplasm of the kidney. It has been the fashion to insist that the commonest cause of unilateral hæmaturia is a neoplasm. It is, however, doubtful if neoplasm of the kidney is as common as has been taught. With this teaching in his mind the urologist has been rendered too anxious, and has been inclined too readily to remove a bleeding kidney in case he might be missing an early neoplasm. The results of removing a large late neoplasm of the kidney are on the whole disappointing, and the only chance of permanent cure resides in making the diagnosis of malignant kidney before the tumour has become so large as to be palpable. Again, it is in the highest degree unwise to open a kidney at operation to see if it contains a neoplasm. If it does and if it has been opened, recurrence within a year or less is almost invariable. If a surgeon is to get permanent results and any real cures of neoplasms of the kidney, he must make up his mind as to the diagnosis before he starts the operation, and must remove the kidney intact within its perinephric and fatty capsule. If the capsule is torn—apart from any incision of the kidney—an early recurrence is the rule rather than the exception. These considerations have led urologists in the past twenty years to remove a large number of kidneys suspected of neoplasm when none was present. A large number of these cases were in all probability cases of purpura.

Fortunately a way of escape can be seen. Let it first be recognized that neoplasm of the kidney is comparatively rare and is by no means a common cause of hæmaturia. Pyelography, repeated several times, if necessary, should invariably be carried out in all cases of unilateral hæmaturia. If the pyelogram shows no evidence of neoplasm, it should be trusted, the patient kept under observation and the kidney left alone. The chances are that the bleeding is a purpura confined to one kidney and may be repeated a number of times. Provided the hæmorrhage is not alarming no harm can be done by waiting and taking repeated pyelograms at intervals of two to three months. In some cases the hæmorrhage is so severe as to endanger life, and it will be necessary to operate. In seven cases I have had to remove the kidney for grave hæmaturia due to purpura, and in one of my cases of purpura of the bladder a bleeding kidney had been previously removed by another surgeon. I am certain I have left *in situ* quite a number of purpuric kidneys, where I have observed unilateral hæmaturia and repeated pyelograms have been negative. In some cases the hæmaturia has been repeated several times before clearing up, in others it has never been repeated. I have also removed a certain number of profusely bleeding kidneys wherein no purpuric lesions could be seen in the pelvic mucous membrane, but where on section a certain amount of interstitial hæmorrhage was apparent lying between the tubules (see fig. 2). I believe that these cases should be classed in the same group and should be considered as instances of interstitial hæmorrhage into a viscus caused by purpura or "the hæmorrhagic disease."

Differential Diagnosis.—The differential diagnosis from other causes of vesical bleeding, especially hæmorrhagic or tuberculous cystitis, is readily made by the cystoscopic observation of petechiæ scattered throughout the bladder, in between which the mucous membrane appears healthy. The differential diagnosis from other causes of renal bleeding is more difficult. Common causes such as infection by the colon bacillus or the tubercle bacillus, calculus and hydronephrosis, are detected by the usual routine methods. Less common causes of renal bleeding are a high systolic blood-pressure, which may be associated with petechiæ on the skin, and with or without "granular" kidney; the various anæmias and leukæmias; and polycythæmia. A careful examination of the blood, including the clotting time, bleeding time and a platelet count should be made in all cases of hæmaturia. The size of the spleen should be estimated by palpation, percussion and X-ray examination. It must be clearly emphasized that in all cases of hæmaturia a most rigid and exhaustive study must be made of the blood. By this means not only can cases of thrombocytopenia be marked off and if necessary treated by splenectomy, but it may also be possible to separate off cases of aplastic

anæmia, pernicious anæmia, leukæmia, cholæmia, and early cases of polycythæmia. I have met with three cases of polycythæmia where profuse unilateral hæmaturia was the earliest symptom. In the first I removed the bleeding kidney, in the other two I was able to make the diagnosis by examination of the blood, taught by experience of the first case.

Scurvy may be mistaken for purpura and is in all probability an instance of a true purpura where the cause is known, namely vitamin C deficiency, due to lack of fresh fruit and vegetables. The platelets are not deficient in numbers.

Hæmophilia can usually be distinguished owing to its hereditary nature, its history and the fact that the clotting time of the blood is delayed, whereas the clot itself is normal and there is no deficiency of blood-platelets.

Hæmoglobinuria is distinguished by expert examination of the urine.

One of the commonest causes of profuse hæmaturia is acute pyelitis. The sudden onset with a rigor and *high* fever, the presence of *pyuria* as well as bacilluria, the enlarged *tender and painful* kidney and the quick response to alkaline treatment should differentiate pyelitis from purpura.

Prognosis.—In the twenty-four cases analysed, the sixteen vesical cases all recovered quickly, four of the nephrectomy cases recovered completely, two of the nephrectomy cases still suffer from mild recurrent attacks of hæmaturia but are definitely improved, and two died in a few months despite nephrectomy. Stephen Mackenzie [13] states that most cases of purpura recover in the end, but that 15 per cent. die chiefly from nephritis, endocarditis, or loss of blood.

Treatment.—In eight of twenty-four fulminating cases and cases with grave hæmaturia it was necessary to resort to nephrectomy. In the mild cases, especially in children, the most likely treatment to prove efficacious seemed to be to give 25 c.c. of antistreptococcic serum by the mouth every forty-eight hours for two or more doses, and to attend to the teeth and tonsils. The serum when given by the mouth did not appear to lead to anaphylaxis, and it certainly produced as profound an effect as when given under the skin. Calcium lactate appeared to have no ameliorating action. Possibly an active preparation of parathyroid gland with calcium might give better results. In all cases it is probably wise to give large doses of alkalies according to Blum.

In relapsing cases most marked benefit was obtained in the majority of cases by giving antistreptococcic serum by the mouth three times in a week every two or three months. At the same time all teeth shown by the X-rays to be diseased were dealt with in easy stages, and the tonsils, if diseased, were enucleated. In one case a heavily infected appendix was removed and cured the trouble, and in two others an intestine heavily infected with *Streptococcus fæcalis* received treatment and with the diminution of the streptococcus in the stools the tendency to hæmorrhage disappeared.

Autogenous streptococcal vaccines were used in two cases. In small doses they did no harm, but effected no real improvement. If the dose was too large it at once produced an attack of purpura.

If no local focus of bacterial infection can be detected in the teeth, throat, upper air passages and bowel, resort should be had to other methods, which will be discussed below. The simpler methods should be employed first, and the more severe methods employed only when these have proved unavailing. Briefly, these measures in order of increasing severity are: Auto-sero therapy, direct transfusion of homologous blood, protein shock therapy and splenectomy.

ÆTIOLOGY OF PURPURA.

The Blood-Platelets and the Spleen. Experimental Considerations in Men and Animals.

Denys, a Belgian histologist, in 1887 called attention to the fact that in some cases of purpura there was a low platelet count. Hayem [14], in 1890, confirmed this and made the following observations:—

(1) That there was no appreciable change in the red blood-corpuscles.

(2) That there might be a considerable diminution in the number of platelets and that those present might be of "giant type."

(3) That there was no constant change in the leucocytes.

(4) That the blood coagulated in normal time, but that the fibrinous reticulum developed as fibrin of unusual size, and did not retract from the walls of the glass vessels into which the blood had clotted and did not squeeze out the serum from the clot.

In 1912 Duke [15] called attention to an additional fact—that though the clotting time was normal, yet the bleeding time of a pin-prick might be considerably prolonged. A prick which should cease to bleed in three minutes might bleed for as long as an hour. He studied the platelets in thirty-one cases, and in fourteen he found a low platelet count below 65,000 per c.c. of blood, the normal being 200,000 to 300,000. If the platelet count was below 10,000 the case was severe, if below 1,000 very severe.

Ledingham and Bedson [19] advanced these observations further by work on guinea-pigs, rats, rabbits and goats. They showed that an anti-guinea-pig platelet serum produced purpura in guinea-pigs, producing also an early extensive fall in the platelets; if recovery ensued the platelets rose again to normal. The effect was specific and was not produced by heterologous sera. An anti-platelet serum had no effect on the leucocytes, an anti-leucocyte-serum had no effect on the platelets, yet both would produce a partial clumping of the red blood-cells. Anti-platelet serum contains a specific antibody for platelets, and this supports the view that platelets are independent elements of the blood and bear no relation to the red cells or leucocytes. Platelets appear to supply an indispensable thrombogenetic element, and, if reduced, the animal is liable to suffer from purpura. These results have since been confirmed by Lee and Robertson [20], Gottlieb [21], Watabiki [22]. Duke [15] produced purpura in rabbits by repeated injections of diphtheria toxin and benzol, both of which agents destroy platelets.

Purpura in man has been noted after injections of salvarsan (Anwyl-Davies [23], Labbé and Langlois [24], Wydooghe and Ferond [25]). It has also been observed in benzol poisoning (Anderson, Boyd and Jackson [26] and in iodine poisoning (Stephen Mackenzie). I have observed it in two cases after injections of streptococcal vaccine.

General purpura has been provoked in rabbits by repeated doses of X-rays (Lacassagne, Lavedan, de Léobardy [27]).

Frank called the attention of clinicians again to the low platelet count in some cases of purpura and elaborated the term thrombocytopenia for this class of case.

Kaznelson [28] observed a case of purpura with thrombocytopenia where the spleen was enlarged. Arguing that the enlarged spleen might be actively destroying the platelets, he had the spleen removed at operation by Schloffer, with complete cure of the patient. In 1918 and in 1919 [29, 30] he reported further cases of successful splenectomy for this trouble. Hitzrot [31] reported further cases, and Edwin Beer [32] reported five cases of splenectomy for this class of purpura, four of which were successful, and states that some fifty cases have now been reported in the literature of splenectomy for thrombocytopenia with the hæmorrhagic diathesis or purpura. He considers that splenectomy can only be of avail in purpura recurrens and not in purpura fulminans. In some of Beer's cases though the number of platelets increased after splenectomy, they dropped again in course of time; but the hæmorrhages did not recur and the patients appeared to be cured. Brill and Rosenthal [33] noted the same after two cases of splenectomy. This fits in with the observation of Service [34] who cured a case of diabetes with low platelet count of the bleeding tendency by means of insulin and repeated blood transfusions. Yet the blood-platelets remained low. Beer could produce no evidence by examining the blood from the splenic vein and artery that the spleen did destroy platelets. Yet the removal of the spleen appears to remove the tendency to hæmorrhage.

The heart of the problem still awaits solution. There is some key to the experimental puzzle yet to be found. Brill and Rosenthal suppose that the spleen must in some way cause the capillary walls of the blood-vessels to become sensitive to circulating toxins. They say the platelets are not directly concerned as a cause of the bleeding tendency.

Beer suggests: (1) That there is a defective formation of platelets in the bone-marrow. (2) That circulating toxins destroy the platelets. (3) That the spleen destroys the platelets. None of these hypotheses covers all the facts.

Spence [35] analyses 101 published cases of splenectomy for purpura. The bleeding tendency was cured in sixty-nine, and twenty-one died of the operation. He agrees with Beer that splenectomy is suitable for chronic relapsing cases only. He divides the cases into three types in an ingenious attempt to formulate a theory of the action of the spleen and reticulo-endothelial system in causing purpura.

Giffin [36] reports a number of cases of unusual types of hæmorrhagic disease from the Mayo Clinic which serve to show that the problem of causation can best be solved by further research on clinical cases.

Conner and Bumpus [59] conclude that there is not enough evidence at hand to prove that essential hæmaturia is ever localized purpura, or due to a deficiency of blood-platelets, but the evidence is rather suggestive that this is true in some cases.

Local Infective Foci as a Cause.—It would appear that there are several different types of purpura, with differing causation, but that in a number of cases of purpura a local focus of infection can be found if carefully sought. The removal of this local focus may cure the tendency to hæmorrhage. The infection is most likely to be due to a streptococcus, but it may probably be due to any bacterium, such as the colon bacillus, *Staphylococcus aureus*, pneumococcus, meningococcus and the viruses of small-pox or measles. The local focus is most likely to be found in the teeth, tonsils, accessory air sinuses, middle ear or bowel.

Bradburn [37] reported a case of purpura cured by removal of septic teeth, and in a number of the cases reported above and in those reported by Moreland McCrea [18], the removal of septic teeth or septic tonsils appeared to lead to a cure. In three of my cases purpura developed the day after the extraction of septic teeth, and in another after the removal of septic tonsils. Similar happenings have been reported by Kleeblatt [38] (teeth), by Robson [39] after the removal of a rusty nail from the foot, by Kretschmer [6] after an operation for osteomyelitis, by Clay and Golden [40] after an operation for mastoiditis. Wadsworth [41] reported a case of bilateral renal calculi with streptococci and pyuria that developed purpura. I have observed two cases of severe purpura in women associated with pyelitis due to the colon bacillus. In each case renal lavage cured the condition.

It seems clear then that local infective foci may cause purpura, and that the removal of these, if not too roughly carried out, may be followed by a cure.

The Results of Injections of Serum, Blood and Foreign Proteins.

Weil [42], in 1905, showed that in cases of hæmophilia the blood could be rendered normal for a time by subcutaneous injections of normal horse-serum; surgical operations could be safely carried out in hæmophilics after the injection of horse-serum, and bleeding could be stopped in the same manner after operation in hæmophilics who had not previously had injections of serum. When house-surgeon at the London Hospital in 1906 I first employed horse-serum with success according to Weil's advice in a case of hæmophilia that had inadvertently been operated on and was bleeding dangerously; and have since used it successfully in a number of cases.

Nolf [43] in 1909 showed that bleeding in hæmophilics and in hæmoglobinurics could be stopped by subcutaneous injections of peptone. Widal [44] found that similar results could be obtained in some cases of purpura; that injections of serum and peptone stopped hæmorrhage at once and if repeated might cure these conditions.

In a number of the cases reported above subcutaneous injections or oral administration of normal horse-serum or of antistreptococcic serum have been employed. Experience has shown that in the majority of cases the remedy quickly checks the hæmorrhage. Repeated injections greatly diminish the severity of the attacks and render recurrences less frequent. Yet in some cases despite repeated injections the attacks continued to recur, it is true in a less severe form and at longer intervals, but a complete cure does not always appear to be attained.

Widal [45] announced later that the action of the serum or peptone was probably non-specific and acted by producing a colloido-clasic crisis; that any foreign protein introduced into the circulation might produce a favourable result, even the injection into a muscle or under the skin of the patient's own blood which apparently acts as a foreign protein (auto-sero-therapy). However these injections act there can be little doubt that they should be the second line of attack in dealing with purpura. Favourable results have been reported in purpura after the subcutaneous or intramuscular injection of horse-serum (Stern [46], etc.), antistreptococcic serum, peptone, sterilized milk (Gram [47]), and even the patient's own blood (Widal, Emsheimer [48], Howard [49]). Yet the results are not uniformly successful. Resort may then be had to intravenous injections of whole human blood from a suitable donor. Should such treatments prove ineffective, then the question of splenectomy should be considered, as brilliant results have been reported in a number of cases. Splenectomy has so far been reserved for cases of true thrombocytopenia, and should only be employed in severe recurrent cases, not in simple or fulminant cases. Giffin's recent work suggests that splenectomy may sometimes be considered when there is no thrombocytopenia.

Some writers have reported good results from subcutaneous injections of adrenalin in repeated doses. Others state that small doses of turpentine may do good.

Morris [50] reported a case in China in 1916 cured by emetine hydrochloride; another successful case was reported by Plantier [51] of Algiers.

Blum [2] and Szabó [3] advise large doses of alkalies in cases of bladder purpura to render the urine alkaline. They state that urine contains pepsin which in acid urine may cause digestion of the hæmorrhagic areas and the formation of "peptic" ulcers. The alkali is said to render the pepsin inactive.

Oppenheim [52] states that he cured a case by radiation with a quartz lamp.

Suggestion has been employed in the cure of hysterical cases (Schindler [53]).

The Classification of the Purpuras.

Attempts to classify cases of purpura on an ætiological basis must as yet be incomplete, for in at least one-third of the cases no light whatever can be thrown on the exciting cause. Nevertheless, a partial classification based on our present knowledge is more helpful than the older attempts on a clinical basis. For instance, Stephen Mackenzie, and to a less extent Osler [54], seek to divide the cases clinically according to the historical description of Werlhof [55], Willan [56], Henoch [57] and Schönlein [58], as follows:—

(1) *Purpura Simplex.*—In young persons, with lesions confined to the skin, and which soon clears up by natural process of repair.

(2) *Purpura Hæmorrhagica (Werlhof).*—A more severe type associated with high fever, a tendency to recur that may prove fatal, and where hæmorrhages are observed not only in the skin but also in the mucous membranes, joints and viscera. The hæmorrhagic lesions may undergo necrosis and lead to ulceration and gangrene.

(3) *Purpura Rheumatica (Schönlein).*—In persons who appear to suffer from so-called acute rheumatism, associated with symmetrical tender hæmorrhagic swellings in the limbs, with slight fever, lasting several years, seldom fatal, and where the heart is often affected. Yet the disease does not appear to react favourably to salicylates.

(4) *Henoch's Purpura (Willan).*—Occurring chiefly in childhood, associated with intense abdominal colics and vomiting, swellings of the joints, albuminuria and hæmaturia, with slight fever, recurring over several years, and seldom fatal unless attended by severe nephritis.

Osler states that the skin lesions can be of four kinds: Purpuras; serous effusions; erythemas, diffuse or nodular; necrotic areas. The disease has two outstanding features, the recurrence of attacks at long and short intervals, the morphological inconstancy of the skin lesions. The visceral lesions are of two types, mechanical, due to exudation of blood; and inflammatory, such as nephritis of all grades of severity, less often endocarditis, pleurisy and even peritonitis. The ætiology is dual: (1) Infections; (2) perverted metabolism of the nature of anaphylaxis.

Attempts to classify the purpuras too closely on a clinical basis seem apt to lead to confusion. The simplest way to look at the condition is to realize that purpuric bleedings in any situation are only a symptom and not a disease; that adequate classification will only become possible when a large number of different causes that may give rise to the symptom of purpura have become adequately recognized and proved; that purpura in the skin can be associated with bleedings into any mucous membrane or viscus, and that the cases can fall clinically into three main groups, simple, recurrent and fulminating. The best classification so far attempted appears to be that of Brill and Rosenthal. This has been somewhat modified below in the light of further clinical observations made in the last few years.

In the first place, all cases of purpura can be classified by an examination of the blood into two main groups: (1) The thrombocytopenic; (2) the non-thrombocytopenic.

In both it is possible that injections of sera, blood and proteins may do good, but it is only in the first group that splenectomy has so far been employed and may bring a cure.

In the second place cases of purpura may be classified into: (1) those in which a proximate cause is apparent and which it may be possible to remove; (2) those in which the cause is unknown.

32 Kidd: *Purpura of the Urinary Tract*

(1) *Those in which a proximate cause is apparent.*

(*A*) *Bacterial Poisons.*—Streptococci, staphylococci, pneumococci, meningococci, smallpox, measles, acute rheumatism, local infective foci in teeth, tonsils, sinuses, middle ear and bowel, trench nephritis (Stevens and Peters), pyelitis.

(*B*) *Chemical Poisons.*—Turpentine, quinine, belladonna, iodine, benzol, arsenic, salvarsan, snake venom.

(*C*) *Intrinsic Metabolic Poisons.*—Cholæmia, anaphylactic agents.

(*D*) *The Poisons Generated in Diseases of the Hæmopoietic System.*—The leukæmias, aplastic anæmia, pernicious anæmia, Banti's disease.

(*E*) *Vitamin Deprivation.*—Scurvy, rickets.

(*F*) *Functional Changes in the Walls of the Blood-vessels.*—Schindler has reported two cases in victims of religious mania which were cured by suggestion.

(*G*) *Changes in Blood-pressure.*—High blood-pressure, senile purpura, purpura of the menopause.

(2) *Those in which the cause is unknown, so-called idiopathic purpura or the hæmorrhagic disease.*

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